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ROYAL SOCIETY OF MEDICINE

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JOHN NACHBAR, M.A., M.D.
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THE EDITORIAL COMMITTEE

VOLUME THE FIFTH

SESSION 1911-12

PART III

ODONTOLOGICAL SECTION	OTOLOGICAL SECTION
PATHOLOGICAL SECTION	SURGICAL SECTION
THERAPEUTICAL AND PHARMACOLOGICAL SECTION	

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PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

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COMPRISING THE REPORT OF THE PROCEEDINGS FOR THE
SESSION 1911-12

ODONTOLOGICAL SECTION



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ODONTOLOGICAL SECTION.

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The Council think it right to state that the Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Odontological Section.

October 23, 1911.

MR. H. LLOYD WILLIAMS, President of the Section, in the Chair.

PRESIDENTIAL ADDRESS.

GENTLEMEN,—My first duty and privilege on assuming the Presidency of the Odontological Section is to express to the Council and the members my pride and my gratitude for the honour they have conferred upon me, and my humility in the contemplation of the long list of gifted men who have been my predecessors in the chair.

Former Presidents have from time to time taken for their theme some portion of the historical field of odontology; the contributions that have been made will be found to be of the greatest assistance to a future historian to obtain the correct perspective of the movements which have assisted dental art and science to the position it obtains to-day.

I am able to look back upon twenty-five years of professional life, for that has now elapsed since I took the Membership of the College of Surgeons, and it is quite surprising to find what wonderful strides surgery has made in that comparatively brief time. The surgery of the kidneys, associated with the name of Sir Henry Morris, had developed markedly, but it was new and by no means generally practised. Abdominal surgery was in its infancy. I remember the sensation that was caused while I was a student by the publication by Spencer Wells of his first 100 consecutive cases of ovariectomy without a death. Brain surgery was only commencing its wonderful development.

The carbolic spray was still used while operations and dressings proceeded at some, though it had been dropped at several, hospitals in London. No antiseptics were used in the ordinary extraction room at Leicester Square as a routine practice when I was a student, but we were taught the free use of water in the washing of the instruments. Mr. Moon, especially, insisted upon scrupulous cleanliness; he was particularly

careful to notice the hands of the operators. After some time an open dish containing carbolic lotion heated over a spirit lamp was allotted to each chair; the instruments were at first more generally dipped into this solution, than thoroughly disinfected before or after using. This constant evaporation of carbolic lotion made the room a much safer operating room than it would have been with its heavy curtains separating the chairs. Boiling the instruments was at first a complete failure, because almost everyone was against it, and the house surgeons *would not* under the circumstances become enthusiasts: the instruments got into a dreadful state. The idea then was to boil all the instruments before the day's work began, and as they were used, to ensure a degree of disinfection from the hot carbolic lotion, and again to boil them at the end of the day's work. Following this, closed sterilizers were obtained, heated by spirit lamps; the water in these was, as a rule, hot. In course of time all the sterilizers came to fulfil their purpose and their meaning. I have sketched this gradual development because it may some day be interesting to know some of the steps by which aseptic dental surgery grew to its present strong position.

Septic infection and septic periostitis following extraction are now as rare as they were formerly common. This great improvement—for it is a great improvement—has not been brought about by the use of antiseptic mouth-washes, or by the use of scrupulously sterilized extracting instruments. Preparation of the part and its neighbourhood for operation is as essential to success in dental as in general surgery. Infection, when it does take place, can but rarely be caused by an unclean instrument, it is almost invariably due to the presence in the mouth of other septic foci. Preparation of the mouth, then, and especially the thorough cleansing of the gums, has secured this triumph.

It is a source of gratification to many that the gums are coming to their own. The teeth received all the attention of students in the past: how to fill them best. In every way we learnt, and in my opinion very well, too, what was possible to the saving of the crown of the tooth. I remember one of the ablest operators I have known saying to me one day, "I have only recently completed a large number of gold fillings for a patient and now the teeth are getting quite loose."

If the older text-books are compared with the latest text-book in this country, the most striking difference noticeable is the space now devoted to diseases of the gums and periosteum, and to oral sepsis (a term which I trust to see discarded). Already a considerable amount of work in this field has been accomplished. One very significant conclu-

sion is that which ascribes caries of the teeth and inflammation of the gum margin with its numerous consequences to the same cause—the collection of foods and débris on and about the teeth.

Stagnation areas are in the main due to loss of function of dental organs. It is well recognized that those organs of the body which are not sufficiently employed deteriorate organically, and frequently become the seat of disease; this fact applies equally to the dental tissues—a tooth which has for any reason lost its function becomes more liable to caries. But the gums around such a tooth are immediately attacked, for the delicate gingival margin cannot tolerate decaying and fermenting food in contact with it. In the principle, therefore, that a tooth which has lost its function should be removed or have its function restored dental surgery has made a decided advance. The wise application of this principle will lead to a great improvement in the teeth of the nation, it will bring about a diminution of caries of the teeth and will conduce to that essential of good health—a clean mouth.

A clearer classification of diseases of the gums and periosteum is rapidly becoming possible; every marginal gingivitis is not our old friend pyorrhœa alveolaris. There is the curable group in which, though undoubtedly forming a formidable group under the term "oral sepsis," thorough cleansing, removal of calculus and restoration of function entirely removes the trouble, and recurrence can be surely guarded against by a little instruction in mouth hygiene. The other group, in which destruction of the periosteum and caries of the bone are the special signs, still demands much patient study and observation. This Section has added largely to our knowledge; we have every reason to be proud of the patient investigation into the bacteriology and the pathological anatomy of this subject which members of this Society have already made, and happily continue to make. Bacteriology and pathology agree that in the main the symptoms which are attributed to this group of dental diseases are due to the sepsis, and treatment converges, therefore, upon the question how to remove the sepsis and prevent its return. At present there is no distinct agreement in the answer. There is one fact which dominates the position and will continue to limit the efficacy of any remedial treatment, that is, that the periosteum once destroyed cannot be reproduced.

In another field of investigation, that into the ætiology of dental caries, the period under review has been most fruitful. Miller's announcement that he had artificially produced dental caries which was in no way distinguishable from the lesion that occurs in the

mouth was given to the world during my student days. Very valuable work on the bacteriology of caries has since been carried out in this country, and chiefly by members of this Section, work involving an enormous amount of diligence, patience, and the greatest accuracy. As our knowledge of the ætiological factors has increased, attention has been more and more focussed on methods of prevention. Undoubtedly great progress has been made in the increase of our knowledge of what may be termed the physics of the oral structures. Proper food, by adequate exercise, ensures the free nourishment of the structures during growth, and as the suitable food also assures to the hard and soft tissues hygienic surroundings, it gives promise of their health and functional preservation.

The influence of oral conditions upon the health has received the closest attention for many years. Blood diseases, such as severe anæmias, are attributed to septic conditions of the mouth. Whether ultimately all that has been claimed against sepsis of the mouth will be generally conceded by medical men or not, the ventilation of the subject by means of so many articles, based on patient observation, has certainly drawn general attention to a possible and very probable source of infection. Many intestinal diseases, such as gastric and duodenal ulcers, are said to be caused by infections from the mouth. It is certain that some such cases show an immediate and marked improvement after thorough cleansing of the mouth, though the treatment may have involved some loss of blood from extraction; after the immediate marked improvement of the first three days the subsequent course of the illness shows more gradual improvement. This seems to indicate that a close relationship exists between the oral state and the general health, even though it may not prove what is the immediate cause of the illness the patient is suffering from. It is our constant experience that people suffering from illness due to sepsis improve rapidly in health and increase in weight after the removal of all their teeth.

The pneumococcus, we know, is a normal habitant of the mouth. Certain classes of illness in which this coccus is predominant occur in circumstances which render the possibility of the infection arising from the mouth a reasonable probability. It sometimes happens that a patient recovering from typhoid fever is attacked by pneumonia: it seems highly probable that the second infection is from the mouth. Middle-ear disease, in which the pneumococcus is again the chief offender, not infrequently follows the exanthemata and other debilitating diseases. Stomatitis during the exhibition of mercury in the treatment of syphilis

in the secondary stage is very distressing, and frequently incapacitates the patient. If the mouth of the sufferers were thoroughly cleansed at the commencement of the treatment, and then kept clean, there would be probably very slight trouble or none at all. Even when the condition is severe, the immediate improvement following the removal of all local irritation, whether from food débris, tartar, roots, or teeth, is surprising. Much may still be done to improve the lot of patients during illness by strict attention to the hygiene of the mouth.

Tuberculosis has been receiving greater attention from the general public of late than any other disease. No efforts that can be made to remove this disease can be too far-reaching. There is one very serious fact in the history of tuberculosis—that tuberculosis attacks young adults at the period of their life when their vigour is greatest. Baginsky has satisfied himself that the infection passes through the tonsils of children and lies dormant until adult life. If this view is correct, may it not also be true that the infection passes through the mouth? That it is possible for the tubercle bacillus to pass through to the submaxillary glands has been shown. The close association which numerous papers read before this Section have shown to exist between adenoids and the condition of the teeth, gums and lips, renders even the suspicion that such a ravaging disease as tuberculosis may have its beginnings in the unhealthy state of the tissues of the mouth as well as the throat a matter of the gravest import.

The study of the gums, the periosteum, the alveolar bone, and the root of the tooth, in health and disease occupies the same position in the minds of odontologists as caries of the teeth in the past; diseases of the gums and periosteum have a more profound effect upon the general health than caries of the teeth; they are more subtle, often painless, and frequently very extensive. The attention, when specially directed to the gums, is not withdrawn from the observation of caries of the teeth, for both conditions are produced in dirty mouths. Also early attention to simple hygienic rules, combined with the selection of appropriate food, forms the prophylactic treatment of the one as well as of the other of these diseases.

The views concerning the relative importance of caries of the teeth as such, and inflammatory affections of the gums and periosteum, which I have endeavoured to place before you in their historical bearings, are of peculiar value at the present time. The nation seems to be moving rapidly on the path of social amelioration. One phase of this movement is embodied in the Bill for the medical examination of school children,

another in the National Insurance Bill now before Parliament. In the examination of school children much greater stress must be laid upon the condition of the children's gums, but not less on the state of the teeth. In all questions of insurance the condition of the gums and periosteum are of the utmost importance in arriving at a just and equitable judgment upon the value of the life of the individual examined.

Mr. FAIRBANK, in proposing a vote of thanks to the President for his address, complimented him on his moderation. He said the subject of cleanliness of the mouth was one of great interest at the present time. Though the disinfection of instruments was of great value, it appeared to him that a great deal more depended upon the innate cleanliness of the dentist while operating. He considered that an operator ought never to put an instrument into a patient's mouth without seeing that the cutting edge of that instrument was clean. This mechanical cleansing of instruments was of infinitely more importance than disinfection. With regard to the treatment of pyorrhœa, when he was in Paris, prior to 1870, the French people attended the surgery for the purpose of having their teeth cleansed, though they avoided taking baths; the English people, on the other hand, taking baths morning, noon and night, kept their mouths in a very dirty state. It certainly was a very difficult matter to get patients to keep their teeth clean; in fact it was almost impossible. After cleansing the teeth of a patient, the patient would come again a week later, and behind the lower incisors and in parts difficult to get at, the necks of the teeth would be covered with a mass of microbes. With reference to the treatment of gums, he could not see there had been any particular advance since 1870. At that time suppuration between the teeth and the gum was treated by thoroughly removing the tartar and passing up carbolic on a piece of orange wood, and the patient was given the orange wood and carbolic to treat himself. He had had a patient for forty years who suffered from pyorrhœa the whole of this time; she was now aged 97, and had only lost two or three teeth during the forty years. He called to mind a patient sent by a specialist to have his remaining teeth out, thirteen of them. He himself would not have had one out, but he extracted five of the worst. When his own views were put before the specialist he replied, "Unless Mr. Fairbank can guarantee that the mouth is kept clean, the patient must have the rest of his teeth out." Accordingly the remaining teeth were removed, the poor man was maimed for life, and his eyes were no better. There was a great craze amongst the medical profession in connexion with pyorrhœa; they often did not distinguish between slight, innocent cases of pyorrhœa and a bad attack of rheumatic inflammation with suppuration in a person whose blood was absolutely impure, and who had been suffering from chronic pyorrhœa for years. Owing to the dental profession having pursued such a conservative policy for the last ten years, saving every possible root and every septic tooth, there had been a regular crusade on the part of the medical profession in connexion with the condition of the mouth.

The Presence of Blood-vessels in the Enamel Organ of the Kangaroo.

By A. HOPEWELL-SMITH, M.R.C.S., L.D.S.

MR. HOPEWELL-SMITH showed four lantern slides of photomicrographs of the jaws of foetal kangaroos, in which blood-vessels were clearly visible passing into the enamel organs of the developing teeth, a matter of some importance on account of its bearings on the calcification of enamel and the formation of fluid in dentigerous cysts. The sections had been described elsewhere by Dr. Marett Tims and himself.

DISCUSSION.

MR. GABELL said if Mr. Hopewell-Smith had a series of sections in order it might be possible to trace the course of the blood-vessels. It seemed to him that all those shown had been very near the external epithelium, and not running across to the centres of calcification. They might be the little papillæ, which it was well known dipped into the outer surface of the enamel organ. He would like to know if Mr. Hopewell-Smith had traced the course of these small vessels at all.

MR. F. J. BENNETT congratulated Mr. Hopewell-Smith on his success in tracing out the blood-vessels, and urged him to continue to search for them. It was perhaps a little significant to find them in marsupial dentition, because it was possible it might be an illustration of the condition existing in the earlier forms of development of the teeth. He believed it was Dr. Leon Williams who pointed out that blood-vessels were to be seen in the enamel organ just beneath the stratum intermedium. It would be interesting to know of any branches from the blood-vessels to the cells, and to discover whether they were really adventitious or had to do with the formation of the enamel. The whole question of the formation of the enamel was extremely obscure and no one had been able to say how much was physiological, how much physical, and how much chemical.

MR. HOPEWELL-SMITH, in reply, said it had occurred to him that perhaps they were really protuberances in the stellate reticulum, but they appeared very infrequently, and the papillæ which were seen so well in the cow or calf were quite absent in the sections he had shown. About 1,600 sections were made altogether, through the entire jaws, and in only about five or six were the tube-like structures to be seen. The idea that they contained blood did not strike him at first, but on very careful examination it was thought that

some corpuscles could be distinguished in situ. The tissue was sent by a friend from Melbourne, and kept in spirit during the long voyage, and naturally deteriorated very much. There was no reason why the kangaroo should have no vascular supply in the enamel organs. The rat had such a supply, and he thought if human specimens were examined serially from the front to the back of the mouth there would be traces of blood-vessels in them.

Demonstration of some Pathological Conditions of the Mouth.

By J. G. TURNER, F.R.C.S., L.D.S.

(1) MODEL showing the developmental position of the lower incisors of a child aged $3\frac{1}{2}$. It is the common deformity of the temporary dental arch. The incisors make a Λ shape, reproducing the developmental positions, probably from lack of growth of the jaws.

(2) Model showing the upper jaw of the same child. On the left side there is seen gemmation of the temporary central and lateral, and one can also see that the gemmated teeth are a good deal smaller than the two separate teeth. It is not a common condition among temporary teeth.

(3) The model of the mandible of an adult, showing dichotomy of the left lateral incisor. On counting the teeth we find the normal number between the canines, and one of them is broad, with a well-marked vertical fusion groove; this is not gemmation, but probably dichotomy of the tooth-germ.

(4) Model showing a not uncommon shape of the lower premolars; the two second premolars are flattened from side to side. In some cases they recall a carnassial tooth.

(5) Model showing symmetrical involution variation of the upper third molars; both upper third molars being merely small cones.

(6) In this model the upper lateral incisors have taken on themselves a conical involution shape; the first permanent molars are large, and there appears to be an extra cusp on the inner side. The other cusps are irregularly distributed, and it is impossible to point to the normal fifth cusp. The second molars show prolongation of their cusps. This is probably a degeneration change. Of course the coning of the incisors may equally be an involution change; but together with the coning of the molars I take it to be a degenerate case.

(7) In this model, lying on the posterior part of the crown of the third left lower molar between the two cusps, there is a little nipple-like process. This is not merely a bit of gum that has been left at the time of eruption, but it is a nipple that closely resembles those accessory auricles one gets close up to the lobes of the ear on the outside of the face. I have seen the same condition on the gum over the first permanent left lower molar, and over the second permanent left lower molar, so that this is not an isolated case. I have also seen symmetrically on the anterior pillars of the soft palate, about half-way up, similar nipple-like projections. I cut sections of one of those that existed on the gum of the lower jaw, and I expected to find the well-marked artery vein that one finds in the accessory auricle, but I found nothing but fibrous tissue and small blood-vessels. I regard them as in some way connected with development, probably in connexion with the fissures of the face.

(8) Two upper third molars, in both of which decay is commencing at the same point. They are from a girl aged 23. The point where decay is commencing is on the posterior cusp, where it rests against the cheek, and therefore is never cleaned. It shows the symmetry in the onset of caries, which is quite a marked feature of the disease, and which, of course, means that both sides of the mouth are exposed to the same stress of stagnation.

(9) An upper first premolar with a living pulp. It is taken from a man aged 70, who had suffered from pyorrhœa for a long time. The tooth split vertically along its centre in his mouth, a fact which shows the brittleness of pyorrhœa teeth.

(10) A case of absorption of roots due to pyorrhœa. The absorption always begins at the apex, which is a curious and interesting point. It is often, as here, very smooth, giving rise to suspicion of fracture when the tooth is taken out.

(11) Another case of pyorrhœa absorption; the specimen shows how easily one can mistake it for a fracture.

(12) This specimen shows that the view I am advancing is correct. The end of the root is smooth, and the pad of new-formed fibrous tissue that filled in the space vacated by the absorbed root is still in situ lying close against it. I cut a piece off for microscopic purposes, to see whether any trace of an absorbent agent could be discovered, but could not discover it.

(13) Specimen of a molar, which a few months before had undergone amputation of the buccal roots for the cure of chronic abscess;

10. Turner: *Demonstration of Pathological Conditions of Mouth*

one had been only partly amputated. The disease remained and the tooth had to be taken out. It shows that these things are more easily talked of than done.

(14) Irregular exostosis of left lower premolar roots, from a patient suffering from pyorrhœa alveolaris. The condition is not at all uncommon, and presents great difficulties in extraction. The roots had to be chipped out of the bone; there are little knobs and ridges of new-formed cementum. Possibly there is also inostosis of the surrounding bone. In this patient there was very considerable sclerosis of the bone, and it required a surgical operation to get rid of the teeth, which were septic. I have several other specimens of the same condition.

(15) Sheath-like growth of new-forming cementum, surrounding the dead apices of a lower molar, and joining the two together. Eventually, if growth had gone on, there would have been a large cementoma, formed of new inflammatory cementum, which might have been called an osteotoma or cementoma, and classed with the odontomes.

The PRESIDENT said Mr. Turner had undoubtedly done a good deal to illustrate the pathology of pyorrhœa alveolaris in the past. He referred to a paper which Mr. Turner had read before the Section in 1908,¹ when he exhibited to the Section a specimen of a tooth which had broken during extraction and described the fragility of the teeth in this condition. Possibly many members thought they had observed the fact before for themselves when it was thus pointed out. The benefit of patient observation was very great.

¹ *Proceedings*, 1908, i, p. 105.

Odontological Section.

November 27, 1911.

MR. H. LLOYD WILLIAMS, President of the Section, in the Chair.

Fistula of the Antrum closed by Sliding Bone-flaps.

By FRANK COLEMAN, M.R.C.S., L.D.S.

THE subject of this communication is a man, aged 29, whom I first saw in September of this year.

History: He gave the following history: Towards the end of February, 1911, he had an upper back tooth removed, the extraction of which proved to be a difficult one, and the ends of the root came away encased in a layer of bone. The patient described this bone as having a smooth surface (evidently a portion of the antral floor). Following the extraction, there was a good deal of bleeding from the wound, and afterwards a slight but continuous "watery" discharge from the tooth-socket. This "watery" discharge continued, and patient consulted a chemist, who advised the antrum to be washed out with a weak solution of carbolic acid.

Condition on admission: On September 28 the patient came under my care at the Royal Dental Hospital, and the following condition was then noticed. In the region of the left second upper molar was an opening into the antrum, about the size of a goose-quill, through which fluid could be projected into the left nostril. The antral cavity was small, as a director bent at its terminal end to the extent of half an inch could be made to touch either of its four walls. This manœuvre, to some extent, excluded the presence of a foreign body in the antrum, and gave some information as to the condition of its lining membrane.

12 Coleman: *Fistula of Antrum closed by Sliding Bone-flaps*

The patient was advised to have an operation, with the view of closing the aperture; for although he did not suffer much discomfort, it was a constant annoyance at mealtime, and on occasions such as blowing the nose. At the same time it was explained to the patient that the attempt might result in failure, and even leave a larger aperture than then existed. Before deciding on this operation, there were two points to determine:—

(1) That the normal opening of the antrum into the nose was patent, or else closure of the abnormal one would result in failure, owing to want of an exit for its secretion.

(2) That no foreign body was present in the antrum.

The first of these conditions had already been satisfactorily demonstrated by syringing through the antrum, and the clearness of the returned fluid was a further favourable point.

The presence of a foreign body was excluded by radiographing the antrum with a probe in situ.

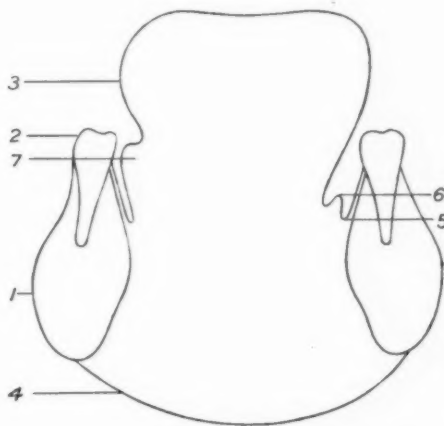
Operation: October 13—After washing out the antrum with boracic lotion, the patient was anæsthetized with nitrous oxide and ether. The edges of the fistula were freshened with an antrum perforator, after which chisel cuts were made into the bone in front and behind the fistula, and similar cuts on its inner and outer surfaces, but with bone forceps. These incisions were made sufficiently deep to weaken without detaching the bone, so that the opening into the antrum was now surrounded by four movable or hinged bone-flaps, which, by means of the thumb and fingers, were crushed together. The operation was completed by uniting the mucous membrane with two silk stitches.

After treatment: October 19—Stitches removed. Wound healing well. No discharge from antrum since its closure, and patient has suffered no discomfort. October 26—Soft tissues have granulated well together. November 9—Left upper second premolar found to be septic, and was removed so as to avoid possible infection of operation wound. November 16—Condition remains satisfactory.

An Important Sign in the Diagnosis of Fracture of the Jaw.

By FRANK COLEMAN, M.R.C.S., L.D.S.

I AM not going to burden you with the signs attributed to a fracture, whether of the jaw or elsewhere, but call attention to a condition which I have found of great service when the usual signs of fracture of a jaw are either absent or difficult of detection.



Coronal section through jaw and tongue in premolar region, showing: (1) body of mandible; (2) premolar tooth; (3) tongue; (4) deep cervical fascia; (5) reflection of mucous membrane from jaw to tongue; (6) sublingual fold (normal condition); (7) sublingual fold distended with effused blood, forming the characteristic swelling beneath tongue.

In a paper which appeared in the *St. Bartholomew's Hospital Journal* for June, 1910, on "Some Points in Connexion with Fractures of the Jaw," I made the following statement: "There is one sign which is almost pathognomonic of fracture of the body of the mandible, and that is an effusion of blood into the (tissues of the) floor of the mouth, raising its mucous membrane and producing a characteristic bluish, tense swelling under the tongue. This alone will differentiate an external bruise from one which has, in addition, caused a disunion of the jaw; and it is difficult to see, from an anatomical

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point of view, how an effusion of blood can take place into this space, bounded externally by the deep cervical fascia, unless a breach occurs either in the latter structure or in the jaw itself. I have never seen this sign referred to, but have found it to be almost invariably present soon after the injury."

The importance of this sign, as I have already indicated, lies more in the exclusion of a fracture than in its actual diagnosis, as most fractures of the jaw are easy of detection.

A case in point is one at present under my care. A patient attended the Dental Department at St. Bartholomew's Hospital on October 21, 1911, and gave an account of having received a blow on the left side of his face five days previously. Although there was marked bruising on this side of his face, there was no sign of a fracture, but, on examining the opposite side, I at once detected the characteristic bluish, tense, raised mucous membrane of the floor of the mouth, and, on further examination, found other signs of fracture of the jaw present.

I do not deny that these alone would have been sufficient to have diagnosed his condition, although the deformity was but little marked; mobility and crepitus of the jaw not easily obtained, and interference with its function was not a prominent symptom.

We are frequently consulted in hospital practice by those who have sustained injuries to their jaws and teeth as to any damage they may have incurred to these parts, and the condition to which I have drawn your attention is a help in the diagnosis of the former.

I regard this sign of effusion of the blood into the tissues of the floor of the mouth as comparable to a discharge of blood from the ear or nose, or an effusion of blood into the orbital tissues in fractures of the base of the skull, and of equal importance as a diagnostic guide.

The sign is only of value within the first week of the injury, as the effused blood becomes absorbed. Most patients, however, suffering from fracture of the jaw are usually seen within this period.

I have no doubt that many have observed and regarded this sign as one concomitant with a fracture of the jaw, but I do not think sufficient attention has been drawn to it as a diagnostic aid. It is a sign which is easy of detection, and I believe almost invariably present, and I make this statement on the examination of some fifty cases of fracture of the jaw which have passed through my hands.

DISCUSSION.

Mr. JAMES wished to know in what cases the author regarded it as important to close the antrum with a flap operation, because it seemed to him that in a very large number of cases they closed quite easily. As the case mentioned was one of nine months' duration there might be some peculiarity which made it persist. With regard to the fracture of the jaw, the point of diagnosis appeared to be a very valuable one.

The PRESIDENT (Mr. H. Lloyd Williams) said that there were many cases in which it was important to have some definite sign, and it was valuable to be able to say, if the effusion was not present, that there was no fracture. He had had during the last week the diagnostic value of the X-rays brought to his notice in a case of fracture he had treated for some time. The patient had a very septic mouth which it was difficult to get him to keep clean, and a long time elapsed before any union occurred. Union had now taken place for about three weeks, and as soon as he was satisfied that such union had occurred he took the splint off. A radiograph was taken of the fracture, and the fragments were shown quite apart. The important point was that when taking a skiagram of a fracture the callus did not show for some months. The fractured ends were seen quite clearly, but the callus could not be seen, while clinically the fragments were firmly held together.

Mr. COLEMAN, replying to Mr. James, said his case had the following favourable features for this method of treatment: The man had had the fistula for nine months, there was no appearance of its closing by itself, the normal opening into the antrum still remained patent, and fluid syringed through the antrum returned perfectly clear. There were other points which rather favoured this particular form of operation—viz., the fact that there were no teeth in the region, so that the bone around the aperture was fairly pliable, and the perforation being on the summit of the alveolar ridge gave some spare bone to work with. It was well known that a large number of these fistulae closed up by themselves, but in the present case, with everything that appeared favourable for closing up, no attempt at closure had taken place.

Mr. G. S. GREENFIELD said he had the pleasure of seeing the operation performed, and would like to know whether Mr. Coleman felt quite certain it was the alveolus that had joined up, and not the mucous membrane over the opening to the antrum. If it was merely the mucous membrane there was a very great chance at some future time of its being opened again.

Mr. COLEMAN said he thought there was bony union, from the firmness of the parts. He had a skiagram taken to determine this point, but it was taken through the entire skull and so did not elucidate this question. He was indebted to Mr. Dolamore for the particular method of operation. He described the condition to Mr. Dolamore, and told him he intended to deal with it by stripping up and then suturing the muco-periosteum around the aperture, but Mr. Dolamore suggested crushing the bone together as a more certain method, and it was that suggestion which led him to perform the operation described.

Local Anæsthesia, with Special Reference to Injection Methods.

By A. H. PARROTT, L.D.S.

IN considering the subject of local anæsthesia as at present applied in surgery generally, and in dentistry in particular, it seems to me that, broadly speaking, two main avenues only have proved of any practical value in its production in human tissues, so far as we have at present travelled on the road to its perfection. These are:—

- (1) Extreme cold applied to the surface of the part to be anæsthetized—e.g., a refrigerating spray of ethyl chloride, &c.
- (2) The introduction of various drugs by various methods into the tissues, hard or soft, or both, as the case may be.

REFRIGERATION.

The method of refrigeration with a rapidly evaporating spray (of ethyl chloride, anæsthe, &c.) is, I imagine, known to all of us as one which, prior to the introduction of injection methods, served a good purpose in many ways, but I think I may take it for granted that its use is becoming more and more obsolete, in view of the improvements in methods and certainty to which we have attained in connexion with the second avenue I have mentioned, the introduction of desensitizing drugs into the tissues. I will, therefore, dismiss it from consideration to-night in favour of methods more modern, more efficient, and more generally applicable to the conditions we are called upon to treat in the course of practice, and the operations entailed thereby.

INFILTRATION BY DRUGS.

The methods of introduction of desensitizing drugs into the living tissues, as affecting our special work, may be briefly enumerated as follows:—

- (1) Superficial infiltration or osmosis by application of a drug to the outer surface of the tissues to be affected, with or without pressure.
- (2) Osmosis aided by the electric current (electrical osmosis or cataphoresis),
- (3) Infiltration by injection of drugs.

(4) Infiltration by injection, combined with the use of an electric current.

This classification may be said to include all the varying methods we have in use at the present time, but a more convenient division of the subject may be made for our purpose. The dental operations for which it is desirable for us at times to produce insensibility to pain are certain to be performed upon one of two very distinct classes of structure—i.e., *within* the teeth themselves, or upon the surrounding tissues, mucous, submucous, periosteal, or osseous; that is to say, it may be desired to produce anæsthesia either internal to the tooth or external, whichever may be preferable for the case in hand. For convenience, therefore, I propose to class the methods arbitrarily under the headings of internal and external anæsthesia as applying to the teeth themselves.

INTERNAL ANÆSTHESIA.

The consideration of methods of producing anæsthesia internal to the tooth itself necessarily excludes operations involving the structures external to it, as, though it may conceivably be possible, it is not at present practicable or convenient to extend anæsthesia so produced appreciably beyond the apical foramen into surrounding tissues. Therefore, methods considered from this point of view can be employed only to relieve the sensitiveness of the dentine or pulp, or both, of a single tooth under treatment, and not for extraction or any operation external to such tooth. Broadly speaking, the ways open to us of producing internal anæsthesia are two. These are:—

(1) The application of an anæsthetizing or obtunding drug to the surface of exposed dentine.

(2) The various methods of what is usually termed "pressure anæsthesia."

(1) *Obtundents*.—To obtundents I must make only a passing reference. Amongst them we have an ever-increasing number of drugs and preparations more or less effective, and valuable in their place. Amongst those to which I would give a foremost place are paraform, erythroplein hydrochloride, chloretone (or dentalone), besides all our old and tried friends, desiccation, carbolic, zinc chloride, alcohol, &c. The trituration in a cavity of a pellet of cocaine or other anæsthetic drug has also been recommended. The chief drawback to the employment of most obtundents is the uncertainty of their success and the

loss of time which may be involved, in addition to the possible pain or difficulty of application met with in many cases. It is unfortunate that the most efficacious obtundents are also usually the most dangerous on account of the difficulty of exactly limiting their penetrative power to the desired extent. The different qualities and powers possessed by each I will not attempt to discuss here, except to mention one case of my own which will illustrate the need of discrimination and knowledge in the selection and use of a drug as an obtundent only. The case in point was a lower sixth year molar, the patient a lady, aged about 30; the cavity to be treated a small mesio-approximal one, easily accessible but very hypersensitive, with no approach to an exposure. I sealed in the cavity a drop of erythroplein hydrochloride (50 per cent. in eugenol) on blotting paper under temporary gutta-percha. The patient should have returned next day; the appointment fell through, and a week elapsed before I saw her again. I then found the cavity absolutely insensitive, and the tooth had given evidence of uneasiness. Fearing a dead pulp I drilled through much sound dentine with entire absence of sensation until I reached the pulp, which proved to be alive, but hyperæmic and sluggish in response to stimulus. Rather than run the risk of future trouble I devitalized it and gave the patient and myself all the trouble of an unnecessary root filling, &c. One such experience makes one cautious as to further use of this or similarly powerful drugs, though the fault in this case lay more with the patient than myself. Paraform has lately been highly spoken of as an obtundent. I have used it many times in 5 per cent. strength, but have not had by any means uniform success with it, and I have found that if left in a cavity for more than a few days, the dentine appears sometimes even more sensitive than prior to its insertion. I shall be glad to have this point either confirmed or contradicted by any member present who may have had wider experience of paraform as an obtundent.

(2) *Pressure Anæsthesia*.—Here we have two means of anæsthetizing a pulp at our disposal:—

(a) The simple application of an anæsthetic drug, usually combined with a vaso-constrictor, such as adrenalin, to an exposure of the pulp, followed by pressure exerted with a tampon of wool, rubber, amadou, &c.; an excellent and convenient method when easily applicable. It has the merits of simplicity and effectiveness usually in proportion to its ease of application and accessibility of the cavity, but in my experience it is so uncertain on the points of time and pain-saving as

to be valueless in cases where exposure of the pulp is not markedly present. A convenient form of applying cocaine in this way is to be found in Parke, Davis and Co.'s neurocaine billets. Each billet conveys $\frac{1}{2}$ gr. of cocaine, and moistened with adrenalin is rapid and effective in suitable cases. The chief danger to be avoided with the use of this method is the forcing of irritant or septic matter through the apical foramen.

(b) *High-pressure Anæsthesia*.—We have the forcing of an anæsthetic drug through normal dentine into the pulp by means of a high-pressure syringe, the point of which is inserted into a pit previously drilled in the dentine if a suitable spot cannot be found in the cavity. I have no personal experience of this method, which does not appear to have been widely adopted, and has always struck me as being a risky one to employ for sensitive dentine only, unless the pulp is to be removed, as so delicate an organ, surrounded as it is by unyielding walls, has in many cases very little margin for recuperation, once it has suffered from any unusual pressure, congestion, or possible irritation.

EXTERNAL ANÆSTHESIA.

Turning now to anæsthesia produced externally to the tooth, we come to a much wider field for consideration, including, as it may do, in addition to anæsthesia of the dentine or pulp, any or all of the surrounding structures and the operations to be performed thereon. I have already mentioned the refrigerating method by freezing sprays, and need not refer to it further here. Also, although from the standpoint I am taking, general anæsthesia also comes under the heading of external anæsthesia, I do not propose to bring it into the scope of this paper unless it be for the purpose of comparison.

Parallels in General Surgery.—The methods of local anæsthesia which we have in use in our profession have their parallels in the wider domain of general surgery, where local, regional, and spinal anæsthesia have come so much to the fore in recent years. In endeavouring to widen our outlook upon this subject, as we should in all, it is worth while to look sometimes at the records to hand in medical literature of the progress of local anæsthesia in general surgery.

Spinal Anæsthesia.—The spinal methods, though merely an extension of the principles of local and regional, stand in a category of their own on account of their far-reaching powers and also widely extended dangers. The achievement of spinal anæsthesia is to my

mind a most masterly and daring procedure; masterly when a complete success, but always daring, for short of an injection into the brain substance itself, the risks of more disastrous after-effects can hardly be imagined, including, as they do, paralysis, meningitis, &c. I have had the pleasure recently of studying an extremely able and interesting paper by Dr. W. J. McCardie [8], the eminent Birmingham anæsthetist, upon the subject of spinal analgesia, and its present position in the world of surgery. The paper is an exhaustive résumé from statistics and records of operators in various parts of the world, and Dr. McCardie's summing up I will briefly quote, if you will pardon me the apparent digression:—

From an extensive review of all the literature available to me on the subject, I conclude that spinal analgesia is retrogressing in favour, and is generally only used when there are marked contra-indications to inhalation anæsthesia, and local anæsthesia is not possible. The exceptions are surgeons who have had a special experience of the method in a large number of cases of the same kind. The *proportion of deaths*, as one would expect from the conditions, is greater than in inhalation anæsthesia. The *immediate dangers* are at least as great. The *after-effects* are not uncommonly most severe, affect the nervous system, and on the average are at least as frequent as those following inhalation anæsthesia. Many of them are most persistent and disastrous, though I must say that the English results are much better in this respect than the foreign. . . . In spinal analgesia the chief after-effects are headache, backache, and raised temperature: in inhalation anæsthesia, vomiting.

The percentage of failures in the former is very high. An excessive dose, whether absolute or relative, in the case of idiosyncrasy is more immediately and hopelessly fatal than is one after ether or chloroform, because it cannot be antagonized by mechanical eliminative means. The diffusion of liquid in the spinal canal is very different from that of vapour in the lungs. . . . I place spinal analgesia, as a method of preventing pain, between inhalation and local anæsthesia. Generally speaking, I think it should only be used in certain selected cases.

My reason for introducing this excerpt from Dr. McCardie's paper is that, looking at local anæsthesia by injection in its broadest aspect, we may realize the widest limits to which it has been brought in the alleviation of pain during operation upon the human body, and the greatest dangers that have been encountered in its employment. It is evident that spinal analgesia has aroused a good deal of enthusiasm, and I imagine also a corresponding reaction of opinion, as to its merits. In dentistry we have no parallel to it, unless we consider, perhaps, local

anæsthesia as applied, say, to the Gasserian ganglion, that is, a blocking of a great nerve-centre to cut off sensory communication with all parts supplied by that centre. Such an operation belongs absolutely to the domain of general surgery, and could only be of practical interest to us in isolated cases outside our ordinary routine; but I think that to appreciate to the full the possibilities and drawbacks of even the smallest injections we are in the habit of using, it is necessary to study a little over the borderline as usually defined between dentistry proper and oral surgery, for even such an operation as tooth extraction will occasionally pass that border, and become a surgical operation in the broadest sense of the term.

Drugs used in Spinal Methods.—The technique of the methods of injection used in spinal analgesia are not of sufficient practical interest to us to justify my giving a detailed description of them. There is a point, however, to which we may well give a little consideration, and that is the relative advantages and disadvantages of the various drugs and combinations of drugs which have been or are at present in use for obtaining analgesia by spinal injection, for I think it is a fair assumption that any substance which may be harmlessly injected into the spinal canal or great neural sheaths must be pre-eminently safe for injection into other tissues if so desired. In this respect Dr. McCardie's summary of the records of spinal analgesia up to October, 1910, does not give us much assistance, as although he states that records of many thousands of cases which he had collected had reference to eucaïne, stovaine, and novocain, he does not distinguish between the three. Cocaine he terms the "chloroform" of local anæsthesia, and it is evident that in general surgery it suffers from a bad reputation as far as safety is concerned, which I think is endorsed by the general experience of our own profession. So far I have not succeeded in tracing to what extent the introduction of novocain and the extended use of it have affected the mortality and danger-rates of spinal analgesia.

LOCAL AND REGIONAL ANÆSTHESIA IN GENERAL SURGERY.

The question of relative advantages of the drugs named I shall leave for a moment, to consider briefly the present position of local and regional anæsthesia as practised in general surgery. Here I shall rely to some extent upon the authority of Mr. Charles Leedham-Green [6] of Birmingham, who has had wide practical experience of local anæsthesia, and who in a recent paper on the subject states that he now

performs 35 per cent. of all his hospital operations with these methods, and regards them as yet more valuable means of anæsthesia for the general practitioner. Amongst the operations included in his records are trephining for depressed fracture of skull, removal of cerebral tumours, tumours of both jaws, innocent and malignant, epithelioma of lips, tongue, tonsils, and cheek. I mention these by way of illustrating the severity and daring of some of the operations which are now dealt with under local anæsthetics, and with much advantage, as in no region does the anæsthetist impede the operator to such an extent as in that of the head and face. The proportion of operations is also direct evidence as to the popularity to which anæsthesia by injection has attained or may attain amongst surgeons generally.

Advantages.—Among the various advantages claimed for injection as against inhalation anæsthesia in general surgery I find the following:—

- (1) No anæsthetist necessary.
- (2) No delayed shock.
- (3) No post-operative bronchitis or pneumonia.
- (4) No post-operative poisoning from any drug inhaled.
- (5) No struggling, excitement, or coughing during operation.
- (6) After-vomiting reduced.
- (7) After-pain in wound very slight.
- (8) Patients can take food immediately after operation.

Nearly all these advantages, if obtainable, are equally desirable in dental operations as in others, where it becomes a question of injection versus inhalation anæsthesia, although the gain to us is perhaps of less vital import than where major operations are concerned, in which general constitutional conditions may be of greater relative importance in view of the usually severer shock of operation. Habit and long usage lead us in our speciality, I think, to look upon inhalation anæsthesia almost as synonymous with nitrous oxide anæsthesia, especially since methods of prolonged administrations have come to the fore. But, if anything, we are tempted to minimize the after-effects of gas, as it is seldom that we see anything of our patients after they have left the dental chair, and it is, I imagine, in the experience of most dentists that there are many cases where even nitrous oxide inhalation would preferably be avoided, if an equally satisfactory method of local anæsthesia might be employed. Delayed or post-operative shock in dental operations under general anæsthesia should, in my opinion, be fully taken into account in deciding what method of anæsthesia is to be employed in particular cases.

(3) The third point of post-operative bronchitis or pneumonia is also one of importance, as being a risk which is very freely run in the administration of N_2O .

(4) Post-operative poisoning from drugs inhaled, though it does not affect us so closely perhaps as the surgeon, is a factor we have often to reckon with; one cannot say with any exactness to what extent prolonged administrations of nitrous oxide affect the subjects, but it is well to remember that even with our old friend "laughing gas" there are many cases of what one may term "idiosyncrasy" (a most convenient word, and one that rather resembles our old friend charity, though it can in no way, from our point of view, be regarded as a virtue).

(5) No struggling, excitement, or coughing during operation. This is one of the chief advantages we can wish for in specially difficult dental operations.

(6) After-vomiting reduced; another far from negligible advantage; from the dental surgeon's usual standpoint, vomiting should be absent altogether.

(7) After-pain in wound very slight. McCardie's investigations seem to have led him to conclude that in surgery this advantage is not a fact, and that patients do complain more of their operation wounds after a local, than is the case usually after a general, anæsthesia. Our wounding operations under local anæsthetics usually consist of extractions, and I think after-pain here, apart from pre-existing inflammation or sepsis, has more ratio to the amount of damage done to tissues under operation rather than to the anæsthetic, be it general or local.

(8) That patients can take food immediately after operation is certainly an advantage in dental cases as in others, provided, of course, that the state of the mouth permits it; and there is hardly any doubt, I think, that the patient who can tolerate local anæsthesia well is in better condition for this than one who has taken nitrous oxide or other general anæsthetic.

Limitations.—Turning from these general considerations to more precise and practical points, we have to consider the limitations as well as the advantages of local anæsthetics. The first and foremost is the ever-present bogey of toxicity, a bogey which one is glad to think we are able, in the light of accumulated experience, to observe in truer perspective. Closely related to it is a second and more subtle bogey—idiosyncrasy. That we are getting to closer quarters with them is, I think, evidenced by the fact that in spite of all that has been recorded and remarked over and over again about the dangers of cocaine as an

injected drug, many operators to-day appear to be using it with impunity and confidence. This has been brought about by several factors: The lower percentages of solutions employed, its combination with suprarrenal preparations circumscribing to some extent the action of the cocaine, the use of fresh preparations, and improvements generally in the technique of operation. But the danger-line is still well marked, and often where a local anæsthesia would be preferred, we have to fall back on a general one, as to be successful we might be driven to employ a larger amount of injected solution than safety will permit, having regard to the two limitations I have mentioned—toxicity of the drug, and possible idiosyncrasy of the patient.

DRUGS USED IN LOCAL ANÆSTHESIA.

Touching these points, it seems relevant to consider here the positions which the best known drugs may claim as shown by comparative experiment and clinical experience. In estimating the value of any drug or combination of drugs used in local anæsthesia, three chief points have to be considered:—

- (1) Their anæsthetic action.
- (2) Their toxicity with regard to the general system.
- (3) Their irritant action upon the tissues infiltrated.

Comparative Properties.—It is chiefly with regard to toxicity that cocaine has laboured so long under a bad reputation, and it is to this fact more than any other that we owe the introduction of the well-known though more recent substitutes—eucaïne, stovaine, tropa-cocaine, alypin, novocain, and others. So far as I have been able to ascertain, the most scientific and conclusive comparative experiments which have been recorded with regard to the qualities of these drugs are those of Dr. Le Brocq [5], of Cambridge, a record of whose experiments appeared in March, 1909, in the *British Medical Journal*, which record does not appear to have been seriously confuted by subsequent investigators. It will suffice here for me to mention the following conclusions amongst others drawn from his results:—

- (1) In anæsthetic action stovaine is to be considered relatively the most powerful; alypin, beta-eucaïne, lactate, novocain, and tropa-cocaine are about equal to cocaine, nirvanine inferior.
- (2) In toxic action alypin is stronger than cocaine. Stovaine, tropa-cocaine, novocain, and beta-eucaïne lactate respectively weaker.
- (3) In irritant action upon the tissues experiments showed the

following results: Cocaine caused slight swelling and hyperæmia soon after injection; the part completely recovered. Stovaine caused intense hyperæmia and dilatation of blood-vessels, followed by sloughing. Beta-eucaine showed swelling and thickening about point of injection, followed by sloughing. Tropa-cocaine caused swelling and some thickening, followed by sloughing. Novocain showed no swelling and no hyperæmia. The part was perfectly normal after injection, and remained so.

These experiments, therefore, show that all these drugs except novocain have a greater irritant action than cocaine, and novocain alone is superior to cocaine in this respect. This point of irritant action upon the tissues touches us far more closely in dental operations than it does the surgeon, in whose operations upon other parts of the body a little more or less after-swelling may be of trifling importance and little additional discomfort to the patient. It seems a just conclusion, therefore, to say that novocain for dental purposes is the superior of all other drugs known up to the present time, and that cocaine being less irritant, though more toxic than the others mentioned, takes the second place.

Vaso-constrictors.—The combination of a vaso-constrictive drug with any of the above anæsthetics appears to be equally possible and effective in diminishing toxicity, and increasing or prolonging anæsthetic power; but, according to [Braun 1], most local anæsthetics more or less neutralize the vascular contractile effects of adrenal preparations excepting novocain, which, on the contrary, increases the anæmic effect, and, therefore, needs a proportionately smaller addition of adrenalin or suprarenin to prevent or control hæmorrhage. A distinction is to be drawn between suprarenin and adrenal preparations made from the gland extract, suprarenin being a synthetic preparation, for which it is claimed, and I think justly, that while possessing the same vaso-contractile effect, it is less prone to decomposition and to give rise to toxic effects than the preparations made from the adrenal glands. The value of a vaso-constrictive effect in conjunction with local anæsthesia is very marked in dental operations, the action of the anæsthetic is localized, its anæsthetic effect increased, the induction of anæsthesia hastened, and its duration prolonged, the absorption of the drug into the general circulation being for the time more or less inhibited, and, therefore, more gradual. From this it is reasonable to infer that the danger of subsequent toxicity due to the anæsthetic drug is greatly minimized in cases where any idiosyncrasy to the drug may exist.

Isotonic Solutions.—The last point I shall mention in connexion with the drugs used is the advantage to be gained from the employment of isotonic solutions for infiltration and injection purposes. It may be shown by experiment [4] that blood-cells brought in contact with distilled water rapidly swell up and disintegrate; if instead of distilled water a strong saline solution be used, the cells shrink. But in a solution containing 0.91 per cent. of sodium chloride they neither swell nor shrink. If distilled water replace the blood serum in which nerves and vessels are bathed, the nerves swell, and though they may fail to conduct impulses, the swelling will cause pain. The employment of a solution isotonic with the blood serum avoids this irritative action and also accelerates the diffusion of the injected fluid into the blood serum, thus hastening and increasing the action of the accompanying anæsthetic drug. In this connexion it may be worth while to point out that novocain-suprarenin dental tablets as originally issued by the manufacturers had sodium chloride in combination, and distilled water only was needed to make the solution. This sodium chloride has been eliminated from the tablets, as it was found that they did not keep well; it is therefore necessary now to add normal saline solution to get the best results from these tablets, a point which, so far as I have seen, has not been made sufficiently clear by the manufacturers to the profession.

Toxicity.—The above brief résumé of comparative qualities of the various drugs used in local anæsthesia leaves us confronted after all with the bald fact that all the drugs hitherto discovered are toxic, to a greater or less degree, and that the dose employed, no matter what the drug, must be limited, not by the extent of operation desired, but by the possible danger of toxic poisoning to the patient. In operations upon the mouth and jaws it has always seemed to me that toxic symptoms will appear more readily than they apparently do in operations upon other parts of the body. Whether this is a figment of my imagination or whether it is a fact that injections in close connexion with the branches of the fifth nerve, and not so very far removed from the cranial centres, are liable to produce nervous shock and toxic effects more rapidly than elsewhere, is a point I leave open to argument. Personally, I have always had this danger in my mind when using cocaine, and during my wider experience and freer use of novocain I have not lost signs of it. That complications may occur in isolated cases, even with novocain, in less than normal doses, seems proved by a case of severe cerebral sequelæ following an injection, which has just

been reported by a Birmingham colleague, Mr. Clayton Cooper [2]. The dose used in this case was 8 to 10 minims of 2 per cent. solution, for the extraction of an upper molar; the patient left the surgery apparently well, but toxic symptoms appeared later and proved very serious, though the patient subsequently recovered. It is only just to state that this patient had previously suffered from phlebitis and thromboses, and was, therefore, considered unfavourable for a general anæsthetic. Such cases serve to show us that, as with motoring, it is dangerous to disregard the legal limit, that limit being the safety of the public, or we shall probably meet with trouble where least expected.

Dosage.—With novocain-suprarenin I rarely find a conservative operation which demands more than a dose of two-thirds of a grain, or say 2 c.c. of a 2 per cent. solution. This I consider a safe dose for normal cases, and where extractions are concerned also I am loth to go beyond it. In general surgery the solutions employed most generally appear to be for cocaine $\frac{1}{2}$ per cent., and for novocain 1 per cent.; the dose may range from 30 to 60 minims according to the areas to be infiltrated, an interval of fifteen to thirty minutes being allowed for anæsthesia to supervene. In our work we require prompter action and more limited diffusion, and I think the stronger solution in smaller quantities best achieves this result.

Where multiple extractions in different parts of the mouth are concerned, nitrous oxide easily holds its own, in most cases for two chief reasons:—

(1) The saving of time and nervous tension to both operator and patient.

(2) The gums certainly appear to heal more readily after extraction, where an injection has not been used, especially where sepsis has been present previously, as is usually the case.

In speaking thus generally, however, I must except some cases of difficult extraction of fractured or buried roots. Here a local anæsthetic is often much to be preferred to gas, as it will give the operator time to perform the operation with as much care and little damage to the tissues as possible, and he will have the advantage in many cases of intelligent assistance from his patient. I have on various occasions removed badly exostosed fragments under a local anæsthetic, with the aid of chisels, excavators, and even the engine burr, where under any general anæsthetic extraction would have been almost impossible without very severe damage being done to the surrounding parts.

INDICATIONS FOR LOCAL ANÆSTHESIA.

Summing up the arguments for and against the employment of a local injected as against a general anæsthetic, in extraction work, they seem to be as follows:—

- (1) A local anæsthetic may be preferable in cases:—
 - (a) Where extractions upon one side of the jaw only are involved, and the dose necessary does not exceed the margin of safety.
 - (b) Where time and care are more than usually necessary for a specially difficult root, &c.
 - (c) Where gums are healthy and sepsis or inflammation do not contra-indicate its employment. This point the operator alone can decide in any particular case; one finds with increasing experience that it is more often possible to obtain a successful anæsthesia by injecting into surrounding healthy tissues, bony or otherwise.
 - (d) Where general condition of patient contra-indicates the employment of an inhalation anæsthesia—e.g., cardiac disease, pulmonary or bronchial trouble, goitre, alcoholism, &c. Also in patients of unusual strength or excitability.

INDICATIONS AGAINST LOCAL ANÆSTHESIA.

- (2) A general anæsthetic *per contra* is to be preferred:—
 - (a) Where multiple extractions on both sides of the mouth or both jaws are to be made.
 - (b) In cases where unusual force may be necessary to open the mouth or dislodge a tooth, and it is preferable to have the patient unconscious.
 - (c) In cases where excessive timidity or nervous tension may make the achievement of a local anæsthesia hardly worth while, owing to the psychic strain imposed upon the patient, and possibly also upon the operator. In general surgery this difficulty is often minimized nowadays by the preliminary dosing of the patient with various sedative drugs, to ensure tranquillity during operation.

Mr. Leedham-Green, to whose work I have already referred, states that he uses subcutaneous injection of scopolamine ($\frac{1}{120}$ gr.) and morphine ($\frac{1}{4}$ gr.) and finds that this has a wonderfully tranquillizing effect both before and after operation. A similar treatment might well be adopted in dental cases where difficulties arise with neurotic or timorous patients. In this respect I look upon aspirin in 5-gr. doses

as a mild but useful sedative, and one of the least likely to cause any bad after-effects.

Anæmia.—I am in doubt as to whether one class of patient frequently met with, those suffering from anæmia in more or less pronounced form, are to be regarded as favourable or unfavourable subjects for local anæsthetics. In favour of a general anæsthesia, it is to be said that they usually take nitrous oxide very easily and with little apparent after-trouble; in fact, in many cases it has been my experience that the colour of the patient has improved after an administration of gas. On the other hand, I do not hesitate to employ a local anæsthetic in moderation in such cases, if the operation is within easy limit. I should be glad of an expression of opinion from any present who may have had any marked results in anæmic cases one way or the other. The chief danger to be guarded against is, I think, the employment of too strong a proportion of vaso-constrictive element in the anæsthetic used, as the primary effect may be more marked upon an already feeble circulatory system. In full-blooded patients, on the contrary, the vaso-constrictive action of an injection may be of much value in diminishing and controlling hæmorrhage, both immediate and subsequent.

METHODS OF EXTERNAL ANÆSTHESIA.

Having considered (in somewhat desultory fashion, I fear) the different values of the drugs employed, let us turn now to the methods of their application and briefly consider the technique involved in their employment for the achievement of local anæsthesia for dental purposes. The nature and extent of the operation it is desired to perform, the length of anæsthesia required, and the condition of the tissues, will be the guiding factors in our choice of methods. Those we may adopt for dental purposes may be classed under three headings, differing in technique according to the objective in view:—

- (1) Infiltration by superficial application.
- (2) Infiltration by injection.
- (3) Infiltration by either of above, assisted by electric current.

(1) *Infiltration by Superficial Application.*—Surface anæsthesia through the mucous membrane of the mouth may be produced by simple application of any of the well-known anæsthetic drugs to which I have previously referred, the strength of solution being, however, increased to 5 per cent. or even 10 per cent. in the case of cocaine or novocain. Care must be taken not to allow such solution of the anæsthetic to

trickle down the throat of the patient; otherwise a very uncomfortable, if not dangerous, paralysis of the larynx and vocal cords may ensue, leading to respiratory difficulties and consequent alarm and discomfort to the patient. Such applications will usually need about five minutes or longer to be at all effective, and are useful in such operations as applying rubber-dam, matrices, taking impressions, or to avoid the pain of puncture for injections, &c. Recently mention has been made in a French journal by M. Chavanne of the use of quinine hydrochlorate combined with other drugs. He gives the following formula for application to mucous surfaces:—

R	Phenol				
	Menthol	āā gr. xxx
	Quininæ hydrochloratis		gr. xxii
	Adrenalin puri	gr. $\frac{1}{2}$

This makes a dark syrupy liquid, and where applicable is effective in making the mucous membrane blanch, contract, and become insensitive. I have found it useful occasionally, but, unfortunately, the taste of the mixture is powerful and far from alluring, and the anæsthesia I have obtained has been hardly worth the discomfort. M. Chavanne mentions this preparation as suitable for *all* purposes and operations in which a local anæsthetic can be used, a statement which I fear I am not in a position to endorse. It may have the merit of absolute safety, but it is far from being sufficiently effective for any other than slight surface operations.

The following formula, suggested to me by Mr. Stacey Robinson, of Birmingham, is not so objectionable to the patient and appears to me to be equally, if not more, efficient, and may be used with advantage for the extraction of loose temporary teeth, &c., where only slight anæsthesia is necessary:—

R	Menthol	ʒi
	Phenol	ʒi
	Ol. gaultheriæ	ʒss.
	Ol. cayoph.	ʒxlvi
	Tinct. cannabis Ind.	ʒss.
	Chloroform	ad. ʒj

Cataphoresis.—Generally speaking, however, anæsthesia by absorption through the mucous membranes seems to be very fleeting and superficial with any known drug. The assistance of an electric current, to accelerate and deepen the absorption of the drug, has been a method

often tried and proved successful, but the time involved and the complication of appliances has usually sufficed to dishearten men in busy practice where time is such a ruling factor in the daily routine of conservative work. For this reason I, in common, I imagine, with the great majority, fall back as a rule upon the second method I have mentioned, that of injection infiltration.

(2) *Infiltration by Injection.*—The methods of producing dental anæsthesia by injection I will deal with for clearness' sake under three headings, as I have previously done in a paper published elsewhere [9]. I do not propose to go closely into details of their technique, for which I may refer those interested to a brief excerpt from that paper which I have here with me. The methods described are :—

- (a) Submucous injection.
- (b) Septal injection.
- (c) Intra-alveolar injection.

(a) *Submucous Injections.*—The first method, submucous injection, is so simple in principle and so generally in use for extraction work that lengthy description of it would be tedious at best. I restrict the term "submucous" in this connexion to injections made only into the superficial soft tissues, not into the denser structures of the jaw, though all injections through mucous membranes might, of course, be included in the term. Were it not that time and the safety of the patient are factors to be reckoned with, deep anæsthesia of the denser structures might more frequently be attained by this simple method, by injecting larger doses and allowing more margin for infiltration by osmosis.

(b, c) *Septal and Intra-alveolar Injections.*—The injection of the anæsthetic into the cancellous bone by the septal and intra-alveolar methods have, in my experience, given great advantages in these two respects. Anæsthesia is obtained more rapidly, certainly, and completely without unnecessary diffusion of the drug over an extended area where it is of no value, and can only increase the possibilities of toxicity and after-effects. I do not wish to imply that every injection need be an intra-osseous one; my advocacy of it is for those cases where deep infiltration by osmosis alone may be slow and difficult on account of density of structure and distance to be traversed by the fluid, and as one becomes more at home with the technique, the deeper method becomes more and more useful, as making for time-saving, certainty, and more enduring anæsthesia. The mere fact that the anæsthetic is injected into bony structure conveys to my

mind no more danger than a submucous injection into gum only, assuming that our solution is sterile and non-irritant. If sepsis and sloughing or toxic sequelæ are to ensue they will be just as disastrous in either method, and it is on this account that I give my adherence to novocain for its non-irritant and sterilizable qualities. It is possible that cocaine is a shade stronger as an anæsthetic, but if in the least more irritant, as it appears to be, quite apart from its toxicity, this advantage is more than counterbalanced, at least in oral operations where irritation is so prone to lead to inflammation.

Mr. Hodge's Report.—With regard to the effectiveness of intra-alveolar injection (with the use of the drill-perforation), rather than quote any record of my own I would refer to a report by Mr. Leslie Hodge, of Liverpool [3], upon his first fifteen cases treated by this method, which report appeared in the *Dental Record* for April, 1910. Mr. Hodge gives a tabulated list of these cases, all for conservancy work, showing pain during injection, period of anæsthesia, and pain upon recovery. With your indulgence I will quote his remarks upon the cases:—

Incidentally, the list reveals uniform absence of pain during injection periods of anæsthesia extending from ten minutes up to the end of whatever operation was being undertaken, anæsthesia being still complete and no sensation being experienced when the operation was completed; that the chief operations, which consisted of the preparation of hypersensitive cavities and the removal of living pulps, were carried out quite painlessly, and that it was possible in one case, where a single injection was made, to prepare without pain no less than four cavities, median and distal, in upper bicuspid teeth.

The after-pain is usually conspicuous by its absence, but the point of injection is nearly always painful and inflamed, but not sufficiently so, as a rule, to be serious. In one or two cases, however, which have been decidedly sensitive at the point of insertion, I believe this has been apparently due to movement of the tissues during injection. Mr. Parrott, you will remember, lays great stress upon this point, which, however, is not so easy to carry out as one would imagine. The solution I have used in all cases has been 2 per cent. novocain.

This report from Mr. Hodge upon his first experiences of intra-alveolar injection is, I think, fair testimony to the utility and effectiveness of the method, which I have had the pleasure of demonstrating clinically on several occasions at other meetings, and which my own experience endorses. The point he mentions as to after-soreness at the site of injection is the only adverse one upon which I need comment.

I have advocated not only that the tissues be not moved during injection, but that, wherever possible, the drill-perforation and subsequent injection shall be made into the *immobile* gum tissue. As an extra precaution it is good practice to touch all sites of puncture with a little iodine and aconite before dismissing the patient, or it may be even better precaution to apply iodine before injection, to assist in securing asepsis, as is often done in general surgery nowadays. The main point of the whole method lies in the fact that smaller doses give a more effective anæsthesia than can be obtained with submucous injections alone, and in view of the fact that cases of poisoning even with novocain have been reported, it is of first importance that the danger of toxicity shall be minimized to the utmost. Personally, I have so far, in some hundreds of cases at least, no serious toxic effects to record, but that cases, such as the one I have previously referred to as reported by Mr. Cooper, should occur occasionally amongst the many and varied systemic conditions which patients present, is hardly to be wondered at.

Injection and Electrical Osmosis.—An adjunct to injection infiltration has recently been brought forward in the form of a battery from which an electric current is passed through an injection syringe and solution to a negative pole, made by pads saturated with saline solution and placed over the region of the Gasserian ganglion. The use of a weak solution of beta-eucaine is advocated. So far the limited experience I have had with this double method of electrical osmosis plus injection has been far from satisfactory, anæsthesia, if attained at all, being much slower and more fleeting than that obtained by injection only, but I must give the method more extended trial before I can fairly form a judgment upon its possibilities. I do not doubt its efficacy in principle, but whether it can be made sufficiently practicable and speedy for daily routine to justify the further complication of appliances I am as yet not convinced.

REGIONAL ANÆSTHESIA.

The last method I shall mention is that of regional anæsthesia. I use this term "regional" merely as in contra-distinction to the word local, to imply the anæsthetization of a part possibly distant from the actual site of operation. In general surgery it is perhaps better known as "nerve blocking." In infiltration for sensitive dentine we employ this method in miniature by "blocking" the apical nerve before it enters the tooth by peri-neural injection. By regional anæsthesia I wish to

infer the same operation, but upon a larger scale—that is, the blocking of the larger nerve-trunks. Hitherto such anæsthesia has, so far as I am aware, been practised systematically only for major surgery; and it is usually too difficult, to say nothing of its discomfort, to make it of general utility to us in our more limited sphere of operations. The points at which nerve sensation can be abolished by nerve blocking in the face and jaws are, of course, many, but the only ones which I think are of practical interest to us are:—

(a) Anæsthesia of the Gasserian ganglion.

(b) Anæsthesia of the inferior dental nerve before it enters the lower jaw.

(a) With regard to the technique of anæsthesia of the Gasserian ganglion I shall say nothing here; I have had no practical experience of it, and it must certainly require a more exact knowledge of the anatomy of the parts than the average dentist possesses to bring a local anæsthetic into touch with the three great divisions of the fifth nerve at this point of their union. The far-reaching anæsthesia which would result from such method is rarely, if ever, called for in purely dental cases, and I will not take up your time in discussing it to-night.

(b) Anæsthesia of the inferior dental nerve is perhaps more within the range of practical politics, and as to this method, I will briefly quote again from Mr. Leedham-Green [7] as one I know to have practical experience of it:—

Blocking of the inferior dental and lingual nerves can be achieved by infiltrating the tissue about the two nerves as they lie on the inner side of the ascending ramus of the jaw, just before the dental nerve enters the foramen in the mandible. To do this the needle of the syringe should be inserted under the mucous membrane covering the anterior border of the ascending ramus of the jaw 1 cm. above the grinding surface of the last molar tooth of the lower jaw. The point of the needle must be kept closely in contact with the bone the whole time, and the anæsthetic fluid injected as the needle is slowly pushed onwards for a distance of 3 cm. The lingual nerve is reached first as it lies just behind and to the inner border of the jaw; the dental nerve lies farther back, but is easily found if care be taken to keep the point of the needle in contact with the bone, and the shaft of the needle parallel to the grinding surface of the molar teeth of the lower jaw.

If the injection is successful it soon produces an anæsthesia of the anterior two-thirds of the tongue on that side, as well as of the mucous membrane of the lower lips and floor of the mouth. The molar, bicuspid, and canine teeth are rendered insensitive, but the incisors generally escape on account of their receiving branches from the inferior dental nerve of the opposite side.

These last words of Mr. Leedham-Green's description are interesting to note; if in the course of the discussion for which I hope I have furnished ample (perhaps too ample) material, any gentleman present can enlighten us further from practical experience of this method, I am sure it would be of interest to all, though to most of us, perhaps, merely academic.

In conclusion, Gentlemen, I wish to thank you for the honour you have done me in inviting me to read this paper before you; and trust that, though I may have put a severe tax upon your patience, I have also put at least a small one upon your interest and intelligence, and that the infliction of the first will not suffice to interfere with full and free payment of the second in the discussion and kindly criticism to which I look forward for more enlightenment upon this subject, my interest in which is a better excuse than my knowledge in venturing to bring it before you.

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DISCUSSION.

Mr. STANLEY MUMMERY thought the Section was much indebted to Mr. Parrott for coming all the way from Birmingham to read his most interesting paper. Mr. Parrott was well known as one of the chief pioneers of local anæsthetics in dentistry. He himself had been very much interested in the subject for some years past, and after reading Mr. Parrott's paper in the *British Dental Journal* he tried the injection method himself. Personally he had used local anæsthesia chiefly for extraction work. The intra-alveolar injection method was difficult at first, and considerable experience was needed before one could be certain of getting a good anæsthesia. With regard to post-operative pain in extractions he had found that it was very much diminished, in fact practically absent, after local anæsthetics as compared with general anæsthetics. After an extraction with a general anæsthetic considerable pain was often experienced for perhaps half an hour, whereas after

extraction under a local anæsthetic this was very seldom the case. He could bear out all Mr. Parrott had said with regard to novocain, and since he first tried it he had not gone back to cocaine. With cocaine there were slight toxic symptoms in one out of every three or four cases. With novocain the proportion of cases of blanching of the lips was extremely small. He thought that toxic symptoms were largely a question of the blood-pressure. It was well known that in injecting a local anæsthetic the blood-pressure always showed a fall. Where blood-pressure was high at first, up to, say, 140, no toxic symptoms supervened even after large doses; whereas if the blood-pressure was below 120 toxic symptoms occasionally supervened. It had been his habit to take the blood-pressure in doubtful cases, and if it was below 110, to refuse to use a local anæsthetic at all, because he believed it to be distinctly dangerous in such cases. If the blood-pressure fell much below 100 unconsciousness supervened very quickly.

Mr. STEADMAN said he had used the method for the last eighteen months, and found it the most certain method of producing local anæsthesia. The most extensive operation he had done up to the present with it was the excision of the four upper incisors for the purpose of crowning. In that case he made two labial injections between the apices of the central and lateral of each side, and although all four pulps were alive he was able to cut through the four crowns with a fissure burr, remove the pulps, and put in a dressing, the whole operation being quite painless. He thought it was the only method by which such an extensive operation could be done. He had not had any after-pain. If there was after-pain in general anæsthesia he found 10 gr. of aspirin would always relieve it, and he gave this freely if he thought it likely to occur.

Mr. L. M. BALDING said he had used Mr. Parrott's method ever since he saw his demonstration at Birmingham, and did not think he had had a single failure in dealing with the premolar and incisive region, his failures having been with molars, especially the second and third, both in the maxilla and the mandible. The difficulty he found was in drilling a hole into the alveolus, and he had no doubt this failure had been due to some fault in technique. From the second premolar forward he thought there should be no difficulty in usual cases, but he had failures behind, and had been obliged to fall back on other obtundents, or devitalizing with arsenic.

Mr. F. M. HOLBORN thought a useful point that might arise for discussion was how far there was justification for using the method for simply desensitizing teeth, because that had really deterred him so far from adopting the method at all. No one denied there was always the risk of "idiosyncrasy." Was it not safer to keep to the other methods of desensitizing? It seemed to him Mr. Parrott used the term "anæsthesia" to include what was usually called obtusion, and he mentioned things usually used for obtunding, especially paraform. He himself had used paraform for some seven years and had had almost uniformly excellent results from it. He had never noticed that its

efficacy had passed off when it had been left in the cavity for any length of time. He had had very few deaths of the pulp from its use, not more than two or three in from 500 to 1,000 cases. Even in drilling out all the fissures in the lower molar, where he had used paraform practically neat in small pits drilled for the purpose, and even when it had been left in for three or six weeks he had found the tooth alive several years afterwards.

Mr. F. R. SMYTH pointed out, with reference to what Mr. Parrott had said as to the greater liability of injections made into the gum causing toxic effects, than with injections into other parts of the body, that there was a physiological reason, namely, that the gum was more freely supplied with vaso-dilator nerve-fibres than other parts of the body, thus facilitating absorption. He was indebted for that assertion to Professor A. R. Cushny, who once called his attention to it. He had not had an extended experience of Mr. Parrott's method, having only practised it in one or two cases. In one case he wished to remove the pulp from an upper second bicuspid; he injected between the two bicuspids near the apices of the roots, was perfectly successful in obtaining anaesthesia, and was able to remove the pulp of the tooth. The patient complained of some slight pain in the first bicuspid lasting for two days afterwards, and slight periodontitis developed. About a week after he noticed some change in colour and found there was no response to heat; on drilling into the tooth he discovered that the pulp was dead and he had to remove it. The tooth was a perfectly sound, one, and although the result was not exactly serious it was undesirable; partly on this account, and partly on account of the trouble and time the process took, he had not practised it to any extent. Also he thought that in practice, for the excavation of a cavity in which it was not proposed to remove the pulp itself, it might not always be an advantage to remove all sensation, because there was no indication then as to how clearly the pulp was being approached. When excavating a tooth, to give the patient a certain amount of pain enabled the dentist to know his position in relation to the pulp, and also to form an idea, from the character and duration of the pain, as to whether the pulp was healthy, before putting in a filling.

Mr. WILTON THEW said that although intradental injection was not by any means in general use he thought it had some points in its favour, and, although it was subject, perhaps, to more failures at present than Mr. Parrott's method, he thought it had a future before it when its peculiar technique was a little better understood. It was only useful for the removal of sensitive dentine or of the pulp, there being no effect on the periodontal membrane or surrounding tissues, except a certain anaesthetic effect due to leaking, which rendered the putting on of rubber subsequently more easy. The advantage of intradental injection, he thought, was the absolute impossibility of introducing a dangerous dose of drug in the mouth. There need not be more than two drops of the drug in the apparatus, and a very small amount in the tooth would produce anaesthesia. One advantage of the method was

that there need be no fear occasioned in the patient, the apparatus used having no resemblance to the ordinary and somewhat dreaded syringe: after-pain was absent. A disadvantage was that in many cases a slight amount of sensation remained in the tooth even after considerable pressure had been applied for a length of time. A certain proportion of teeth, also, were apparently impermeable, especially in people who were gouty. The teeth in these cases were also exceedingly sensitive and difficult to inject. There were also cavities in such a position that injection could not be carried out without making a pit into a fresh part of the tooth. In many cases a pit was unnecessary, provided there was a conveniently placed cavity with some softened dentine into which the nozzle of the syringe could be placed. With regard to the possibility of the death of the pulp after forcible injection of an anæsthetic, he had used the method over a period of two or three years and could not point to one such case, although, whenever possible, he always tested a tooth that had been injected some months afterwards.

Mr. JAMES said that when using intradental pressure anæsthesia in order to remove the pulp, he found that where the pulp could not be anæsthetized by using the drug alone, a little weak acid solution for dissolving the drug would produce the desired effect. Novocain, the drug he usually employed, was rendered inert by an alkali, but with the use of acid one could get penetration even where there was some inflammation present. He often used a little aromatic sulphuric acid.

Mr. J. H. BADCOCK had been very interested in the question of the after-effects of local injections. His own experience was not very great, but he had had a larger proportion of after-effects than he liked, although he had used novocain solutions in quite small doses from 5 to 20 minims of a 2 per cent. solution and often a 1 per cent. solution. The after-effects had not been serious in the sense of endangering the patient's life, but had been sufficient to make them undesirable. The most alarming case he had had was spasm of the glottis, which resulted after the injection of a few minims of solution in the region of an upper wisdom tooth. The same thing had happened before to the same patient with an injection of cocaine, but he did not know that at the time. The patient was able to make him understand that brandy would relieve her, and after brandy had been given in a small dose the spasm was relieved. He found afterwards that the patient always exhibited an extraordinary reaction to any kind of drug. Other after-effects he had noticed had come on after the patient had returned home, the patient feeling ill for some hours and having to lie down, and sometimes the effects had lasted for two or three days. For a long time he had held the opinion that solutions of adrenalin or suprarenin were undesirable in extractions because they checked bleeding and prevented the filling up of the socket by a clot, which was so eminently desirable if subsequent sepsis was not to occur. He had one case some years ago which caused him some anxiety, a case of sloughing and secondary hæmorrhage occurring some days

after an operation, and he put it down to the use of adrenalin. He now used novocain generally without adrenalin, and would like to know if Mr. Parrott thought its use in this way was more likely to produce after-effects.

Mr. GABELL was surprised that nobody had remarked on the septic after-effects of injections, because he had seen very ugly-looking wounds, both in private and hospital practice, after injection of the gums, carefully conducted with clean apparatus. Considering the prevalence of infection in the sockets of teeth and how difficult it was sometimes to avoid passing a needle into such pockets, he wondered that more harm did not result. He had no personal experience of intra-alveolar injection himself and had only seen one case in which it was used, a case of an upper left canine in which the injection was given for the purpose of inserting a filling. He saw the patient two months afterwards and found the whole tooth extremely sensitive and hyperæmia extending over the labial surface of the root. He thought the risk of septic infection in the mouth was appreciable and often very serious locally.

Mr. PARROTT, in reply, quite agreed with Mr. Mummery that after-pain was lessened in cases of the extraction of a periostitic tooth, and also agreed that cocaine was more toxic than novocain. With regard to blood-pressure, he always made a point of operating, if possible, when vitality was at its highest point, and preferred to operate within an hour or half an hour after the patient had had food. This was an important point in connexion with local anæsthesia. He was glad to notice that Mr. Steadman endorsed the use of aspirin, which was a very good and harmless remedy. He did not know whether dentists should go so far as to inject scopolamine and morphia, but this had a wonderful effect in quieting the patient before a general anæsthetic. Only a week ago he knew a most excitable and hypersensitive patient who had a beautiful anæsthesia for a long operation, and that was attributed to such an injection. With regard to the difficulty of injecting in the molar region, as described by Mr. Balding, this was a point which only practical experience could solve. Personally, he had succeeded on many occasions in performing an intra-alveolar injection with the drill as far back as the upper and lower second molar, but it was difficult, and the shape of the mouth somewhat governed the possibility. In the molar region local anæsthesia was not quite of so much value, as root canals are often difficult of access; in the wisdom tooth the septal method was very often useful, and it was possible to get up root canals more easily. In the upper region, with a short, stumpy tooth, a needle could often be driven in and a septal injection performed with ease and success. Just behind the crown of the lower wisdom cancellous bone was usually present and was the most accessible spot from which to anæsthetize the lower wisdom. With regard to obtundents, he was pleased to hear what had been said about paraform. He had been careful enough to point out that he did not ignore the use of obtundents. He advocated the use of his method only for selected cases, not for all, but undoubtedly of all the methods of relieving pain it was the one most generally applicable, and the most

far-reaching in its success. He could not quite follow Mr. Smyth's remarks on the superior vascularity of the gum tissue. [Mr. SMYTH said the gum was more freely supplied with vaso-dilator fibres and thus the effect would be quicker than from an injection into another part of the body.] Mr. Parrott said that it was well known that a reflex was obtained almost immediately after an injection, and he had attributed this to the suprarenin or adrenalin acting on the blood-vessels before the anæsthetic had had a chance to take effect. The injection was proceeded with and by the time the second or third minim was reached the reflex had disappeared. He could not see that there was a greater danger of toxicity from a deep injection than from any other. With regard to the dead pulp mentioned by Mr. Smyth, this was a thing he had never experienced after an injection, and he could not at all account for it. If there was any doubt about a filling it was a simple matter to slip a temporary filling in and wait for the patient's next visit to see if there was an exposure. He did not think the patient would agree with regard to pain as a danger-signal to the dentist. There were a few patients who said they preferred to have the pain of excavation rather than the first sensation of fluttering of the heart or the like. He had cured one patient of this by preparing a cavity without an anæsthetic. With regard to the remark as to the trouble and time involved in the method, he might say he employed the method to save time. The moment the injection was completed the work could be done. Frequently for cavity preparation or pulp extirpation a quarter of an hour sufficed for the whole thing from start to finish. Mr. Thew's method of injection was very interesting, and some time or other he hoped to try it, but there was the uncertainty of penetration about it. He had had no experience of Mr. James's method of the use of acid to assist penetration. With regard to the after-effects, Mr. Badcock seemed to have been unfortunate. Spasm of the glottis was an exceptional thing unless some solution trickled down. He had had one or two cases where people complained of lassitude, but he had had no serious effects due to novocain at all. With regard to the risk of infection, he had had only three or four cases of any swelling at all, in each case due to faulty technique. He put this down to the fact of using fresh solutions and taking extra precautions with regard to technique, sterilization of the syringe, &c. Novocain should not be brought in contact with any alkali such as lysol or soda. Alkalis precipitated the novocain very quickly. The syringe should be washed in water, or a saline solution, before using. He did not think it would act sufficiently without adrenalin.

Odontological Section.

January 22, 1912.

Mr. H. LLOYD WILLIAMS, President of the Section, in the Chair.¹

Apparent Symmetrical Bifurcation of the Roots of Upper Temporary Central Incisors.

By A. T. PITTS, M.R.C.S., L.D.S.

IN the case I want to bring before you to-night the teeth were removed for caries from a little girl, aged $3\frac{1}{2}$, at the Hospital for Sick Children. As you will see, the roots are bent forward on themselves and are grooved longitudinally, the groove being more marked on the anterior surface, and the extremities are bifurcated. On extraction it



FIG. 1.

A pair of upper deciduous central incisors showing bifurcation of the roots, which are bent forward.



FIG. 2.

A skiagram of the same teeth to show the pulp canals. The pulp chamber is large and the canals appear to be quite separate.

was noticed that there was a filament of pulp hanging from each extremity. Mr. Clark has kindly taken a skiagram which would seem to show that the root canals are separate, although I am not quite sure on this point. It seemed to me that the case was a little unusual as I have not been able to find any record of similar cases, and therefore I considered it worth while to bring before you to-night.

A Crowned Tooth with a Perforated Root.

By BERTRAM B. SAMUEL, L.D.S.

THE tooth exhibited is a crowned upper lateral incisor, and was removed from a patient aged 65. The crown had been worn for at least thirteen years, possibly longer. There were many other teeth to be removed at the same time and it was thought unnecessary to leave one apparently sound tooth in the mouth. When it was removed it was found that the side of the root was perforated by the post of the crown. The crown is not a very well made one and it seems rather wonderful that no trouble arose from the wearing of the apparatus.

Mr. JAMES said he was partly responsible for the case being brought forward as he thought it was an interesting matter that a tooth should have been thirteen years in a mouth with the post sticking through the inside.

The Brittleness of Teeth removed from Cases of Periodontal Disease.

By J. F. COLYER, M.R.C.S., L.D.S.

IN a communication to this Section on May 25, 1908,¹ Mr. J. G. Turner refers to the fragility of the teeth in cases of periodontal disease and suggests that the absorption of the toxins via the cementum may affect the nutrition of the dentine. I have recently subjected a series of teeth from cases of periodontal disease to staining in borax carmine, and have come to the conclusion that the change that occurs in the tooth is an increase in the calcification of the soft parts of the dentine and cementum. The toxins injure the tooth tissues, with the result that, like other tissues in the body, they react. The reaction takes the form of an increased calcification of the soft contents of the dentinal tubes and cemental lacunæ, with the result of an increase in brittleness.

¹ *Proceedings*, 1908, i, p. 104.

This view is supported by an examination of the teeth themselves. If held up to the light they seem to be more translucent than in the normal, the translucency being most marked about the apex. If teeth showing this condition are immersed for six to eight weeks in borax



a

FIG. 1.

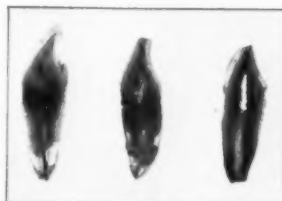
(a) Control. A healthy canine tooth from a young patient.



a

FIG. 2.

(a) Control. A healthy premolar removed for regulation purposes.



a

FIG. 3.

(a) Control. A healthy incisor removed for regulation purposes.

carmine, this translucent area refuses to stain to the same extent as the remainder of the tooth, and this suggests that the soft tissue normally present has undergone calcification. Sections of teeth from three cases of periodontal disease are shown in figs. 1, 2 and 3.

The Treatment of Periodontal Disease.

By J. F. COLYER, M.R.C.S., L.D.S.

THERE is an abundance of evidence to show that oral sepsis is one of the most important aetiological factors in the causation of disease. If we analyse the sources of sepsis in the mouth we shall find that sepsis arising from general periodontal disease is by far the most insidious in its onset and the most serious in its effects.

It is to the treatment of general periodontal disease I wish to draw your attention to-night. Before discussing remedial measures, however, it will be necessary to refer briefly to certain points in connexion with the pathology and clinical conditions of the disease, for on a right understanding of these depends the efficacy of treatment.

MORBID ANATOMY.

On examination of morbid specimens it will be clearly seen that, as far as the alveolar process is concerned, periodontal disease causes a



FIG. 1.

An early stage of periodontal disease.

progressive destruction of the bone, the rapidity of destruction varying in different individuals, and even in different parts of the same mouth, the condition of the bone presenting the appearance of osteoporosis, or rarefying osteitis. The bone lesion is well shown in figs. 1 to 3. In one group of specimens the bone destruction will be found more

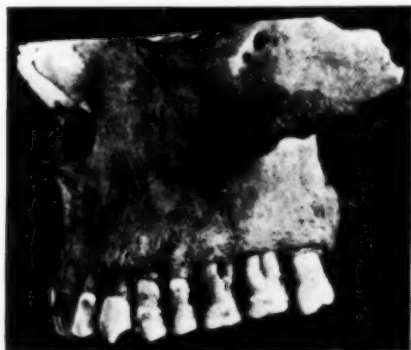


FIG. 2.

A more advanced stage of periodontal disease than shown in fig. 1.



FIG. 3.

An advanced stage of periodontal disease.

marked around the anterior teeth, while in another the principal destruction will be in the region of the molars. Again, there is invariably a greater loss of bone between the teeth than on the labial and palatine aspects, and this is an important point as far as treatment is concerned.

In some specimens the extent of the changes around the teeth appears to be slight, the margin of the alveolar process having receded, but the bone itself presents a sclerosed rather than an osteoporotic condition (fig. 4). In these specimens the arches are invariably well developed, and there is plenty of attrition of the teeth, the latter



FIG. 4.

condition pointing to functional activity in mastication, which is important in its bearing on prognosis, as I shall subsequently show.

The disease is well seen in a variety of domesticated animals and of wild animals kept in captivity, the lesions in the bone being similar to those seen in man.

The patho-histology of the disease, as shown by Znamensky¹ and Talbot,² has its earliest manifestation in the gingival margin, the periodontal membrane and the bone becoming subsequently involved. Mr. Hopewell-Smith³ considers that the primary lesion is in the bone,

¹ "Alveolar Pyorrhæa: its Pathological Anatomy and its Radical Treatment," *Journ. Brit. Dent. Assoc.*, 1902, xxiii, p. 585.

² "Interstitial Gingivitis," *Dental Cosmos*, Philad., 1906, xlvii, p. 1310.

³ "Pyorrhæa Alveolaris—its Interpretation," *Dental Cosmos*, Philad., 1911, liii, p. 981.

but the evidence he produces in support of his view appears to me to be far from conclusive, and his sections may be easily open to a totally different interpretation from that which he places on them.

CLINICAL APPEARANCES.

The earliest stage of the disease is a marginal gingivitis; with the progress of the disease the attachment of the muco-periosteum to the tooth is destroyed, and spaces or "pockets" are formed around the teeth. These pockets, which are usually more marked in the interproximal spaces, vary in depth somewhat in ratio to the severity of the condition. It is the presence of these "pockets" around the teeth that



FIG. 5.

constitutes one of the chief difficulties in treatment. From a practical point of view the depth of the pocket may be taken as an index of the amount of bone destruction.

Clinical appearances are, however, not altogether satisfactory guides as to the extent of the disease, and the amount of bone destruction can only be estimated, with any degree of accuracy, by means of radiography. This is well seen in figs. 5 to 8.

PATHOLOGY.

Briefly stated, a study of the disease in man and the rest of the animal kingdom indicates that the initial stage is characterized by the formation of a stagnation area in the normal space around the neck of

the tooth. Infection with pathogenic organisms rapidly follows, for even in the early stages organisms are present which are known to be associated with chronic forms of disease in other parts of the body. The stagnation area is a septic focus, and destruction of the attachment of the muco-periosteum to the teeth follows. By this process the "pocket" is increased in size, and the periodontal membrane and the surrounding bony attachments of the teeth are progressively destroyed. The rapidity of the destruction depends mainly upon the type of infection and the degree of resistance of the surrounding tissues.



FIG. 6.

Radiograms of the case shown in fig. 5. The fine lines are wires passed into the pockets.

An examination of teeth removed from certain cases of periodontal disease indicates that with the formation of a pocket around the tooth pathological changes commence around the apex of the tooth. This is well demonstrated in the teeth shown in fig. 9. In this case there was a persistent gingivitis, but as far as could be ascertained, neither the pockets nor the bone destruction was very extensive (*see* fig. 10). The teeth on removal showed that around the apices there had been active trouble, as evidenced by the absorption of the tooth tissue which had occurred. This condition can be explained as follows: From the septic focus around the neck of the tooth absorption of toxins or organisms



FIG. 7.

In this patient the trouble was confined to the mandibular incisors and canines. There was marked gingivitis. The patient was a mouth-breather.



FIG. 8.

The radiograms of the case shown in fig. 7. Note the advanced destruction of the bone in the region of the mandibular central incisors.

takes place through the periodontal membrane, probably by lymphatics. I say "probably by lymphatics" because, although histologists have so far failed to demonstrate their presence in the periodontal membrane, on physiological grounds there is every reason to believe they are to be found there. The material absorbed is held up, as it were, in the tissues around the apex. In other words, there is probably a natural defence at this part of the tooth to prevent the organisms and toxins passing into the general circulation. With the arrest of the toxins, &c., the tissues around the apex naturally react to injury; that is to say, the phenomena of inflammation appear. The formation of these septic foci around the apices of the teeth has, so far as I know, not been recognized, but it is clear that it is an important factor to be reckoned with in considering treatment.

WHAT IS A CURE?

I should not have referred to this point but for the fact that opinions differ so widely and so generally as to what is to be understood by a "cure of periodontal disease." This difference of opinion arises in a great measure from the misunderstanding that exists as to what we are to regard as periodontal disease, or, to use the more familiar term, pyorrhœa alveolaris. Many regard the disease as limited to conditions where there is active pus formation, while others hold the view of the disease which I have briefly outlined above. Now, we know by experience, that although active suppuration can be checked in many cases, yet the potential cause of the disease—namely, the "pockets" around the teeth—still remains. Obviously, the disease under these conditions is only checked, not cured, and consequently we are not justified in claiming a cure unless we are able to eradicate all the "pockets," and so prevent stagnation areas. Theoretically, it seems possible to eradicate the pockets—practically it is almost impossible, and actual cures of periodontal disease are therefore rare.

TREATMENT.

What, then, is the problem to be solved in treatment? Briefly, the efficient drainage of the stagnation areas. Before, however, discussing how efficient drainage can best be attained, there are one or two points to be considered in relation to prognosis:—

(1) The important part played by mouth-breathing in the ætiology and pathology of the disease is now well recognized, and it can safely be asserted that local and other remedies will be of little avail while the

mouth is used for breathing. Mouth-breathing acts as a hindrance in treatment by assisting the formation of stagnation areas and by constantly leaving the oral tissues open to infection.

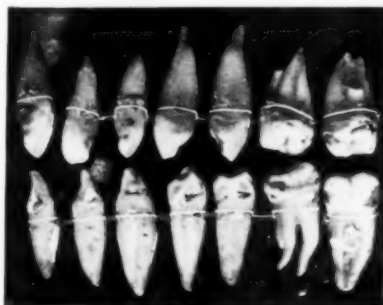


FIG. 9.



FIG. 10.

Radiograms of the maxillary premolars and molars taken immediately before the extraction of these teeth.

(2) The more thoroughly the function of mastication is carried out the greater will be the resistance of the tissues.

(3) The recuperative powers on the part of the patient as indicated by the condition of the alveolar process. The presence of sclerosis of bone may be taken as a sign of resistance.

(4) The condition of the teeth may be taken as an index of the amount of rarefying osteitis. Let me explain this point more fully. Absorption of the hard tissues around the apex of the tooth indicates the presence of periodontitis. You cannot have periodontitis without pathological changes in the adjacent bony tissue. The more rapid the absorption of the tooth the more extensive will be the rarefying osteitis, and the greater the degree of rarefying osteitis the greater will be the liability to direct infection of the tissues.

Turning from these generalities, let us consider more in detail the question of treatment. For this purpose cases may be grouped under two headings—namely, those favourable for treatment and those not favourable.

(1) Cases favourable for Treatment.

The cases favourable for treatment are those where (1) the pockets around the teeth are shallow; (2) the arch is well developed and the function of mastication is efficiently performed; (3) there are indications of recuperative powers on the part of the patient; (4) the patient is a nasal breather.

The treatment resolves itself into a question of drainage. The more thoroughly the pockets can be cleansed the greater the chance of staying the progress of the disease. The measures I adopt are: (a) Thorough scaling. (b) Massage of the gum. By this means, débris, &c., is expelled from the "pockets," and the circulation through the tissues is improved. (c) The regular irrigation by the patient of the spaces around the teeth. For this purpose hydrogen peroxide (vols. xv) is useful. The point to impress on the patient is that the spaces must be kept clear. (d) The occasional use of strong tincture of iodine to the pockets.

These simple measures are sufficient, if faithfully carried out, to bring about an arrest of the disease in favourable cases. I have tried raising the resistance of the tissues by means of vaccines and Bier's method of congestion, but I am extremely sceptical as to the value of such treatment. Thorough cleanliness of the "pockets" seems to be the keynote of treatment.

The two following cases may be quoted as examples where treatment seems to have arrested the progress of the disease:—

M. B. This patient, a well-developed female, was seen early in 1910. There was a well-marked gingivitis, slight thickening of the alveolar process, shallow pockets around the teeth, and a fair amount of attrition of the teeth.

The patient was a nasal breather. She was suffering from indigestion and rheumatism. Local treatment on the lines indicated above was adopted. The patient has lost all her general symptoms and her mouth is healthy. Radiograms taken before and after treatment show that in this case the condition of the bone is stationary (figs. 11A and 11B).



FIG. 11A.

The light appearance of the film taken in February, 1910, is due to over-exposure.

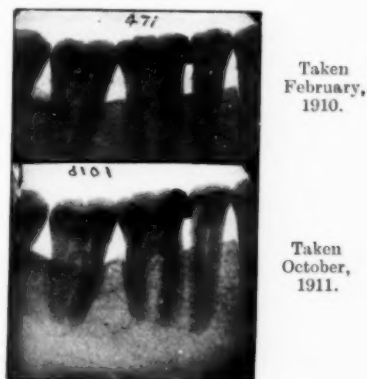


FIG. 11B.

F. S. This patient was a female, well developed, and was first seen in the later part of 1909. The gums were as shown in fig. 12. There was marked gingivitis, no apparent general symptoms. Radiograms showed a fair amount of bone destruction. The patient was a partial mouth-breather; by this I mean she breathed through her mouth during sleep. Vaccines were tried without any irrigation of the tooth pockets. The condition showed no improvement, the discharge continuing from the gum margin. Local measures on the lines suggested were adopted and the patient has very faithfully

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carried out her part of the contract. In this case the disease is progressing very slightly. Radiograms taken at the commencement of treatment and quite recently are shown in fig. 13.

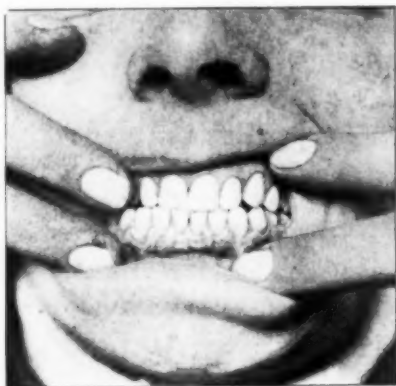


FIG. 12.

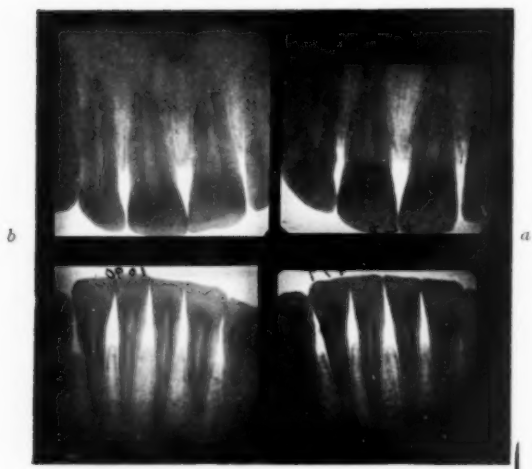


FIG. 13.

Radiograms (a) taken December, 1909; (b) November, 1911.

The films shown in fig. 14 are from a case similar in character to that of M. B. Irrigation of the "pockets" has been adopted in addition to Bier's treatment. The films marked (a) were taken in December, 1908, and those marked (b) in November, 1911. The destruction of the bone is stationary and patient has improved in health, the weight having increased by over 1 st.

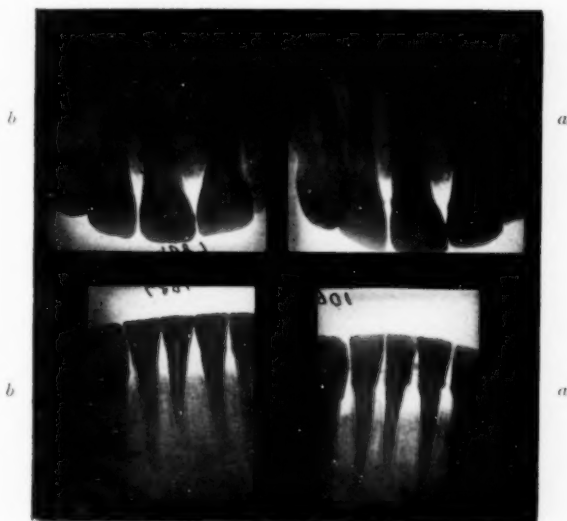


FIG. 14.

(II) Cases not favourable for Treatment.

These cases include those where there are well-marked signs of rarefying osteitis and the general and local conditions are such as to suggest that the tissues have little recuperative power. In this class must be grouped all cases of persistent mouth-breathing. For convenience we may group these under two headings: (a) cases unassociated with apparent symptoms, and (b) cases in which a causal relationship to other diseases has been established.

As regards cases falling under heading (a), there are certain factors which must be kept clearly in mind in endeavouring to arrive at the right line of treatment. The discharge from the tissues may, it is true, be kept in check by efficient irrigation. Possibly also some

advantage may be gained in an attempt to raise the resistance of the tissues by the aid of auto- or hetero-inoculation. All such efforts will, however, fail to stop the advance of the disease. In these circumstances, are we justified in continuing a course of treatment which at the best can only have the effect of somewhat slowing down the progress of the disease? I think not, for two reasons: (a) the patient has a potential source of infection which may become active at any time, and (b) the greater the destruction of the alveolar process the less the chance of making comfortable and efficient artificial dentures.



FIG. 15.

Let me illustrate the first point by the following case :—

F. O., a female, aged 27, was first seen in July, 1909, and came under treatment on account of looseness of the teeth. Beyond slight indigestion she appeared to be in good health. The patient was a mouth-breather. A blood count taken showed a normal condition. The radiograms indicated considerable rarefying osteitis (*see* fig. 15). Extraction was advised, but on the earnest desire of the patient an endeavour was made to treat the condition locally. Three teeth were removed and local treatment and vaccines were tried. When seen in October, 1910, the condition of the mouth was better and the teeth firmer. This patient did not return again until February, 1911, and stated that she "had got tired of local treatment." Her condition was as follows: the skin was blotchy, she was not regular in her periods, she was complaining of gastritis, and felt thoroughly ill. A

blood count showed well-marked anæmia and leucocytosis. The following teeth were removed:—

	6	5	4	3	2	1		1	2	3	4	5	
8			4	3	2	1		1	2	3	4	5	8

She has completely recovered and feels perfectly well. This patient is typical of many we see in practice. The local treatment is carried out at first, but gradually it is dropped and the mouth condition becomes an active focus of infection.

The second reason for early removal of the teeth in cases that are progressing is of practical importance. Let us consider the



FIG. 16.

changes that are taking place in the bone. The progress of the disease means the disappearance of the alveolar process, with the result that, if the disease is allowed to go on to its natural termination, the whole of the alveolar process is destroyed (*see fig. 16*), and from the prosthetic aspect we have to deal with a mouth devoid of ridges on which to steady our dentures. Such cases are unsatisfactory not only to ourselves but also to our patients. If, instead of waiting, we remove the teeth while there is plenty of alveolar process and restore function to the bone by the early insertion of dentures, we shall obtain in the majority of cases a well-marked ridge which will be permanent. Which is the better line of treatment? In cases where the disease is progressing I have no hesitation myself in advising the removal of the teeth. The following case is extremely

interesting in its bearing on this problem. The models marked (a) in figs. 17 and 18 were taken at the age of 40 and those marked (b) at the age of 75. The history of the case is briefly this: The premolars and molars had become loose and had fallen out, and as there was nothing to be gained by retaining the remaining teeth—sixteen in all—they were removed, dentures being inserted. If the models are carefully examined, it will be noticed that where the teeth were lost by the natural cure



a

FIG. 17.

b



a

FIG. 18.

b

of the disease the alveolar process has disappeared, but where the teeth were removed by extraction a well-marked ridge still exists. The early removal of the teeth in this patient has resulted in her having for thirty-five years not only a clean mouth but also dentures which have been steady and efficient.

(b) *Cases in which a Causal Relationship to other Diseases has been established.*—In this group of cases it is absolutely necessary that the oral sepsis should be completely removed. After carefully considering

the cases that have come under my notice during the last ten years I have reluctantly come to the conclusion that the right line of treatment and the only safe course is to remove all the affected teeth. Let us consider the following case, which may be taken as a type. A young adult is attacked with rheumatoid arthritis, and an examination of the mouth shows general periodontal disease accompanied by marked rarefying osteitis. It is a case in which no treatment will remove the potential source of trouble, namely, the pockets. Surely it is better that such a patient should have useful joints and no teeth rather than run serious risk of an aggravated arthritic condition through retaining the teeth. We can supply artificial dentures but we cannot supply new movable joints. In carrying out extraction in these cases I adopt the following procedure: The mouth is made as healthy as possible by a thorough irrigation of the pockets with hydrogen peroxide. The premolars and molars are then removed and the mouth allowed to heal. Models of the mouth are then taken with the incisors in place and bites are obtained. The advantage of this proceeding is that you overcome the difficulty which would otherwise be experienced in arriving at the correct height of the bite after the removal of the front teeth. The anterior teeth are then removed and dentures inserted as soon as possible. The number of teeth which should be removed at one sitting should depend largely upon a consideration of the individual case. Where the "power of repair" is at a low ebb the extraction must be carried out by easy stages, but where there is plenty of "power of repair" the removal may be carried out more expeditiously. I rather incline to the view that very extensive extractions at one sitting should be avoided unless there are special reasons for adopting that course. It is stated that trouble in the bone is likely to follow extensive extractions in these cases unless the resistance of the tissues is first raised by a course of vaccine treatment, but this does not coincide with my experience. I am disposed to think that where there is trouble in the bone as a result of extractions it is almost entirely due to the damage inflicted on the tissues by the operation. There is seldom a rise in temperature following the extractions, provided that the mouth is kept clean. Occasionally a rise in temperature does occur, as is well shown in fig. 19. In that case the patient was suffering from a corneal ulcer and the removal of each batch of teeth was followed by a rise in the temperature.

In cases where general trouble is arising from the mouth it has been my practice to retain the anterior teeth, provided that the bone

destruction is slight. The argument in favour of retaining the teeth in these cases is that the pockets around the anterior teeth are easily accessible and can be thoroughly irrigated by the patient. Experience of these cases has taught me, however, that if the patients are mouth-breathers it is only a matter of time before extraction must be resorted to. The following case is instructive in this respect. Four years ago the premolars and molars were removed for a patient suffering from nasopharyngeal trouble. The remaining teeth were faithfully treated by the patient and the gums, to all appearance, were retained at a fairly normal standard. Three months ago I removed the teeth owing to the fact that the bone destruction was progressing rapidly and I was surprised to find that in spite of all the local treatment there was a large amount of trouble around the teeth. Would it not have been a sounder policy, and much safer, if these teeth had been removed when the original extractions were carried out?

I am aware that treatment by extraction does not find favour with many practitioners and that they are inclined to rely on vaccine therapy. We may therefore with advantage briefly consider how far vaccine treatment can be considered rational in periodontal disease. Vaccine therapy aims at assisting the tissues to defend themselves against the action of bacteria and their products. It is essential for success, therefore, that we should know the causative organism of the disease which has to be treated. There is good reason to believe, however, that periodontal disease is not caused by any special organism; but even if it is due to a specific organism we have not yet identified that organism. In the treatment of periodontal disease vaccine therapy therefore fails to satisfy the most important requirement. It may be pleaded, in favour of vaccine treatment, that the infection in the pockets is causing local injury and that vaccines may raise the resistance of the tissues in the neighbourhood of the tooth. The difficulty here lies in the fact that the infection is invariably mixed, and to be rational the vaccine therapist should prepare a vaccine of all the organisms found. The practice, however, is to use a vaccine of the predominant organism or perhaps of two of them. It seems, therefore, under these conditions, that the treatment is only partial and not complete. But even granting that the vaccine treatment is occasionally successful, the main difficulty still remains, namely, the pockets, and no amount of vaccine treatment will remove the pockets. Putting aside these perhaps theoretical considerations,

we may ask the question, "Do vaccines lead to good results in the treatment of periodontal disease?" I have had personal experience of nearly forty cases of periodontal disease which were treated with vaccines and I can say without hesitation that in no single case was a cure effected and in only a very few cases could I detect any improvement. It is within the experience of all that the majority of cases treated with energetic local measures will show a rapid improvement: consequently when vaccine treatment is carried out concurrently with local remedies and improvement results it is extremely difficult adequately to assess the amount of improvement which should be

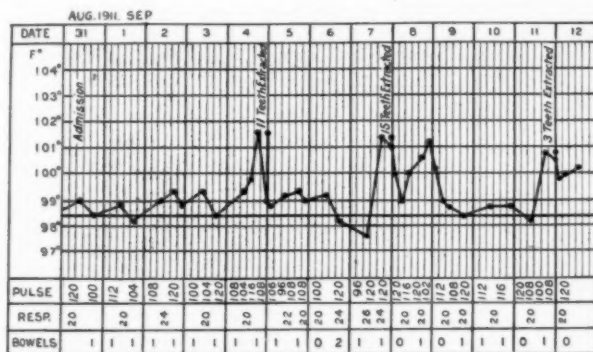


FIG. 19.

ascribed to the local measures on the one hand and to the vaccines on the other.

Personally I have very little faith in the use of vaccines in periodontal disease. In any case it is clear that a cure in the proper sense of the term cannot be brought about by vaccine treatment only. It seems to me that the vaccine enthusiast far too often overlooks the simple elementary principle of surgery, namely, drainage, and still further, is inclined to push his vaccines in the face of active pus formation and increasing general symptoms. I do not wish the above remarks to be read as implying any disbelief in the value of vaccines generally. No one can doubt their value in many cases, but I cannot help thinking that the indiscriminate use of vaccines we see nowadays is likely to bring discredit upon a method of treatment which, when used with judgment, is undoubtedly most beneficial.

Although improvement in the general condition is invariably brought about by the removal of oral sepsis, complete recovery does not always follow. It is, of course, only to be expected that this would be the case, inasmuch as at times there may be other foci of infection which also require treatment, or, what is perhaps more important, the hindrance to complete recovery may be due to the fact that treatment was not carried out until the disease had caused permanent damage. The possibility that the tissues have been permanently damaged must be considered in giving our prognosis.

A word, in conclusion, about preventive treatment. Clinical experience shows that when the disease has obtained a firm hold we have a serious condition to combat. It therefore becomes our duty to prevent as far as possible the onset of this serious disease. We must avoid any operations which may directly or indirectly injure the periodontal membrane. Collar crowns fitted below the gingival margin must not be used. Such a crown injures the tissues around the neck of the tooth and eventually leads to injury of the periodontal membrane. Then bridges of all shapes—removable and fixed—must not find a place in our therapeutic outfit. We must be most careful in adjusting the rubber dam, in the use of clamps, and in any filling operation involving the gingival margin. The treatment of irregular conditions of the teeth must be carried out as far as possible by means of extraction. Regulation apparatus, if used, must be removable and easily cleansed. Fixed regulating appliances cannot be kept clean, and must injure the soft tissues. The wonderful appliances, with their intricate wires, &c., for setting in an ideal arch irregular teeth cause endless damage by injuring the tissues around the neck.

Proper nasal breathing is of paramount importance, and every endeavour should be made to ensure it. Mouth-breathing inevitably leads to periodontal disease.

The patient must be taught from childhood to keep the spaces between the teeth clean by the use of floss silk or any other means considered advisable.

I am convinced that diet plays an important part in the ætiology of the disease. Foodstuffs which require mastication, and which have not been denuded of all their fibrous element, should be used, as such foodstuffs aid the natural cleanliness of the mouth, and, to some extent, prevent the clogging of food débris between the teeth.

As to dental diseases in the future I take a very hopeful view. With increasing experience and fuller knowledge of the ætiology and pathology

of the teeth we shall be better able to prevent diseases and to hold them in check. Caries I already regard as to all intents and purposes a preventable disease, and I am disposed to place periodontal disease in the same category. We are at the top of the wave of dental disease. With a profession possessing an adequate knowledge of the pathology of the teeth, and basing their treatment on that knowledge, aided by the intelligent education of the public, dental disease will, I feel confident, rapidly disappear from our midst, until, perhaps, in less than half a century, from being a universal scourge, it will have shrunk to insignificant proportions.

DISCUSSION.

The PRESIDENT (Mr. H. Lloyd Williams) said the paper had been a very interesting one, covering a good deal of ground; it had given considerable matter for thought, and suggestions which would prove very useful. In the pathology and treatment of the disease the paper gave some distinctly new matter. Perhaps, after all, the most discouraging part to dentists was the conclusion, where Mr. Colyer held out the promise to the public that very soon dentists would not be wanted. Perhaps later on the only place where a dentist might be found would be as a curiosity in a museum.

Mr. F. J. BENNETT said the paper was a very interesting one and expanded many opinions which Mr. Colyer had put forward on other occasions. He was inclined to think that Mr. Colyer was apt to make statements upon too small a foundation, and was encouraged in that belief by the opening remarks of the paper that evening, because Mr. Colyer at once accepted as proved that which was by no means proved—namely, that the translucent zone was one of calcification thrown out by the living dentine. This was an assumption. The question was argued by Dr. Miller and himself many years ago, and he was not aware that any distinct fact had been added since. He was sure there were still points that would be laid before the profession which would add a fuller knowledge of the pathology. He thought that Mr. Hopewell-Smith had something to bring forward which would throw some new light on pyorrhœa alveolaris. To assume that the disease was due to the accumulation of food, or to dirt, really explained very little. Many cases of pyorrhœa alveolaris occurred in people in whom mouth-breathing was absent, for instance, in lawyers, clergymen and others who had had special training in breathing. Therefore he did not see that the matter had been carried very much further by Mr. Colyer. Cleanliness, of course, was a matter of importance, but he was certain a further study of the disease was required.

Mr. STURRIDGE said the able manner in which Mr. Colyer had put the subject before the Society brought him to the front as a great authority on

periodontal disease, and for that very reason he would like Mr. Colyer to explain one or two points which were not quite clear. Mr. Colyer referred rather vaguely to suppuration of the periodontal membrane, and there must be some definite point at which he considered affection of the periodontal membrane to be untreatable. Would Mr. Colyer say that he considered every tooth which had once been affected in any way by pyorrhœa, however slightly, became one which it was necessary to extract? Was he of opinion that it was useless to treat pyorrhœa at all? Would he advocate the extraction of a whole set of teeth where only a few were diagnosed as affected? The fact could not be disguised that there were a great many workers all over the world who claimed to be able to treat pyorrhœa successfully and preserve the teeth indefinitely for periods of from ten to twenty years. These were the teeth of which Mr. Colyer advocated wholesale extraction at first sight. Surely amongst the men who made that claim there must be some honest men, and therefore their statements should be taken into account. The very first slide put on the screen was one which, in Mr. Colyer's opinion, showed the commencement of pyorrhœa, but he himself would say that it was an advanced case. Every radiograph on the screen without exception showed some calculus on the roots which had not been removed. His own idea of treating pyorrhœa and Mr. Colyer's idea were very far apart. It was absurd to talk about treating pyorrhœa by such things as thorough irrigation of the pockets, massaging the gums, local irrigation, and slight sealing. It was impossible to do any good without removing every particle of calculus. He had seen cases in which a little calculus had been left on one tooth and every tooth became healthy except that one. He did not think a tenth of the instruments now made could remove calculus. Mr. Colyer's idea of irrigation was foreign to him; he could not understand how any results could be expected, and thought Mr. Colyer would never obtain good results if he continued on his present lines. The sealing of tartar would not cure pyorrhœa, but it was certainly necessary to scale, and even polish, every tooth. Pyorrhœa should be recognized at the beginning and the calculus removed, because he had never seen a case where calculus had been left in which any improvement had taken place. To extract a whole set of teeth because there was suspected rarefaction of the bone was beyond his conception. He hoped Mr. Colyer would mention the line of demarcation between cases which he considered curable and cases which he considered incurable.

MR. HOPEWELL-SMITH complimented Mr. Colyer on putting so plainly his views on the condition and treatment of pyorrhœa alveolaris. With a good deal of what had been said he was sure members were in perfect agreement, especially with regard to treatment; but he thought it would be generally conceded that treatment of a symptom or a disease was dependent on the pathology of such symptom or disease, and that the pathology was based on an accurate knowledge of the anatomy of the parts concerned. He was not at all clear in his own mind as to the anatomy of the parts concerned in so-called

"periodontal disease." In the first place, very little was known about the gum tissue itself. The so-called glands of Serres in man certainly did not exist in the gum tissue; there was no gingival organ, as described by Black, in man. Secondly, the nature of the osseous foundations of the roots of the teeth had not been sufficiently investigated. He believed that Mr. Colyer spoke about lymphatics in the periodontal membrane and a compact tissue round the margins of the tooth sockets, but there were no such tissues as far as he was aware. Comparing the alveolar processes of the lower animals, the *Felidae* had denser bone than the *Primates*. In the hyæna's jaws could be found solid compact bone wherein the teeth were embedded, but this was diploëtic in man and the anthropoid apes. Again, the anatomical relationships at the margins of the gum were not known with certainty. Dr. Black had described, in sheep, what he called a circular ligament which tightly bound down the gum to the necks of the teeth, but in man he had never seen that ligament. Dr. Black also described a small space which he said was filled with salivary corpuscles. Recently he (Mr. Hopewell-Smith) had been endeavouring to discover whether there was normally a space, and he was able carefully to pass a fine point to a depth of 4 mm. at the neck of a tooth in what might be, and probably would be, a potential "pocket"; there was always a sulcus, a *gingival trough* as it might be called, existing round the neck of every tooth of every man, woman, and child in the country. The next thing he desired to discover was what the trough contained, especially to see if it was possible to find the corpuscles mentioned by Black. He invariably found micro-organisms, and could state that there was a mixed infection in the gingival trough of all persons, young or adults, with normal mouths. Anyone could easily verify this statement in ten minutes. Therefore, in order to have a thoroughly scientific and satisfactory treatment, it was necessary to know the pathology and the anatomy upon which the pathology was based. With a great deal of Mr. Colyer's treatment he entirely agreed. He thought the "pockets" should be irrigated, but he deprecated the practice of passing up a probe from one "pocket" to another, spreading infection every time. The attachments of the soft parts at the necks of the teeth were exceedingly delicate, and often it was better not to probe a "pocket" at all. An X-ray photograph would tell the story without the use of any instrument. He thought it was quite wrong to use an atomizer, which distended the "pocket" still more and carried infection farther in. The pocket was frequently "blown up," and matters were made worse. It was better to create a vacuum by special apparatus and draw the pus out of the "pockets" than blow it farther in.

Mr. W. RUSHTON thought all the members were indebted to Mr. Colyer, who, with his accustomed vigour and sincerity, had brought forward his opinions. Although they might not agree altogether with him, he had opened up a subject which was at least a matter for considerable thought. He himself did not agree at all with Mr. Colyer that the cause of periodontal

disease was known, any more than the cause of dental caries was known; he believed that in both conditions the cause was much deeper than was often thought. Micro-organisms had been in the mouth for countless generations, but as far as he knew pyorrhœa amongst us was a comparatively recent disease. It was well known that in another ancient civilization, the Hindu, pyorrhœa was very prevalent; in fact he was told by a medical missionary that in some parts of India no persons kept their teeth after the age of 40. It appeared to him that, like dental caries, it was a disease of civilization; he believed the intrinsic causes lay much deeper than Mr. Colyer thought, and that until the deep-rooted pathology of the disease was discovered not much advance could be made. He agreed with Mr. Colyer that no good could be done without enlisting the hearty co-operation of the patient, and the first duty of a dentist was to be always on the look-out for any hyperæmic areas on the gum margin, and immediately to call the patient's attention to them and treat them. When teeth were very elongated and loose the wisest plan was to extract them. He certainly disagreed with Mr. Colyer about collar crowns, because his observations, extending over many years, had shown that if properly fitted they did no harm, but he had seen many cases in which an overlapping filling on the gum margin had proved the starting-point of pyorrhœa. He believed that pyorrhœa manifested itself in various ways, some of which were quite distinct. Some cases proceeded with great rapidity, often accompanied by abscess of the gums; others seemed to be so slow in their formation and progress that it required comparatively little treatment of the patient to retain the teeth for many years. He thought in most cases a hopeful rather than a despairing view should be taken, provided the intelligent co-operation of the patient could be enlisted in daily irrigation of the pockets with a neutral preparation of hydrogen peroxide.

MR. STANLEY MUMMERY supported Mr. Colyer in his wholesale condemnation of bridges and gold caps. He himself had not put in a bridge for over ten years, but he had taken a great many out, and had never failed to find filth and septic matter underneath. With regard to focus of concentration around apices of the teeth, he frequently found in cases of chronic pyorrhœa sudden flaring up, and apparently an ordinary dental abscess ensuing without previous death of the pulp. It was possible that the pus was carried up from the gingival margin and that it gave rise to a distinctly circumscribed abscess at the apex of the tooth. He would like to ask Mr. Colyer how he carried out his irrigation of the pockets, whether with an atomizer or syringe.

MR. WILLIAM HERN thought Mr. Colyer's observations on the pathology of pyorrhœa were fairly correct. Mr. Colyer mentioned that the first stage was a stagnation area which subsequently became infected with organisms, but he himself would like to change the positions of these, and say that the first stage was an infection of organisms in the free margin or sulcus of the gum, and the gingivitis which was associated with it was the natural defence of the gums

against those organisms. Infection occurred first and congestion and inflammation followed. This was sometimes observed in the healing of wounds. When wounds healed by primary union there was no inflammatory action at all, but when organisms had access inflammatory action was set up. He considered that gingivitis, which was the earliest manifestation of pyorrhœa or periodontitis, was due to the infection of the natural sulcus of the gum by micro-organisms. He had not observed the septic foci at the apices of teeth which Mr. Colyer mentioned, but he had noticed in the early stages of pyorrhœa alveolaris a certain amount of tenderness of the teeth to percussion, showing that there was a periodontitis spreading further up the root than would perhaps be expected from the appearance of the gum. He did not agree that mouth-breathing was a very important factor in the causation of periodontitis, although he thought it a contributory one. In most cases of mouth-breathing there was a redness of the gum, but he considered that to be due rather to the want of masticatory friction. Many mouth-breathers were cases of superior protrusion, and the frictional effect of the act of mastication was not so marked as in normal occlusions. Apart from this there was also a want of friction of the tongue, for when the mouth was kept open the tongue was not doing its duty as a brush in keeping the mucous membrane swept as it did in a normal case. With regard to general treatment, his own experience agreed very much with Mr. Colyer's; he had found that general treatment by vaccines was practically useless without local treatment, and that when combined with local treatment it was very difficult to say whether the general treatment had increased the effect of the local: he therefore relied on local treatment. With regard to preventive treatment, he strongly supported Mr. Colyer, because he believed such treatment was of the very first importance. No tartar should be allowed to remain on any tooth under the impression that it was a protective. No marginal gingivitis should be allowed to escape our notice, and it should always be promptly treated. The thing of supreme importance in this treatment was to instruct the patient to frictionize the gums so persistently with the tooth-brush that no infection of the sulci could take place. Under such treatment the gums could be kept pale pink, hard and healthy. He agreed with Mr. Colyer about the good effect of massage, but he thought he had missed a very important matter—viz., to instruct patients thoroughly and regularly to frictionize all parts of the gum with the tooth-brush. He considered this the great preventive of pyorrhœa. He did not agree with Mr. Colyer in his views about the baneful effects of crowns and bridges. If these were properly constructed and fitted and the gums properly frictionized, the baneful effects were absent. He could show Mr. Colyer cases of crowns that had been in for very many years where the gum was as healthy about the crowns as in any other part of the patient's mouth.

Mr. H. BALDWIN said there was very little in the excellent paper with which he disagreed, but he did not agree with the wholesale elimination of crowns and bridges. To put the matter in a nutshell, crowns and bridges that

could not be kept dentally clean should not be made or allowed to continue. He believed that pyorrhœa, like caries, was due originally to want of friction on the gum. Through imperfect mastication or improper food the gum lost its tone and became easily infected. The whole disease originated in the infection of the edge of the gum or possibly the edge of the pericementum itself with micro-organisms owing to the gum having become atonic from want of friction: and as the disease progressed the micro-organisms sank deeper and deeper into the pericementum, causing it to ulcerate and the tooth to lose its attachment, and the micro-organisms might in many cases penetrate into the pericementum deeply in advance of the separation by ulceration. The bone became secondarily affected and was removed by absorption. With regard to the cure of pyorrhœa alveolaris, he thought that when under treatment the discharge absolutely ceased and the teeth became much tighter and lost their pain and tenderness to pressure, it might be said that the disease was, for the time being, in abeyance: and if after the lapse of three months or so from the time treatment had ceased none of the symptoms returned, he thought it might be said the disease was cured for the time being. There might be reinfection, but that was another story. The repair of previous damage was also a different question. He did not believe the bone of the alveolar process, when it once had been removed by ulceration or even absorption, was ever repaired at all, and he did not believe the attachment of the pericementum to the root was ever re-established. When cases were cured the gum tightened up to the root, and in some cases so closely that it was difficult to discover there had ever been a pocket there at all. Therefore repair of damage had to be separated from actual cure of the disease. With regard to the cases which should be treated, personally, he thought that in long-neglected cases when they were very bad, when the teeth were twisted about and pushed out of position and loosened, it was as a rule better not to try to cure at all. Where the separation of the pericementum from the root was about one-third of the attachment and where the teeth were not too loose it might well be legitimate to attempt to cure. When after a course of treatment the disease was cured and the teeth remained somewhat loosened, it was very important to fix them by some means, such as stapling, or letting a wire into the teeth to prevent movement. It was very essential to remove all tartar, and as the gum shrank down under treatment and further tartar appeared it should be at once removed with the very greatest care and assiduity. When the tartar had been removed the pockets ought to be cauterized somewhat severely to destroy callous tissue and kill off the part most thickly impregnated with micro-organisms. For this purpose he was very fond of deliquesced chloride of zinc put into the pockets and right round the root. He used a little fine paper-like slip of orange wood in a holder, which was dipped in the deliquesced chloride of zinc and passed gently and with care down into the pocket and around as far as it would go. After cauterization on subsequent days he used chinisol in a pure condition slightly moistened with water and poked down into the sockets day after day with an orange wood slip, reverting to the cauterization if the

discharge proved obdurate. Peroxide of hydrogen he thought was very useful, and in chronic cases he had used the strongest perhydrol. Then came massage and shampooing of the gums, which was a most essential part of the treatment. The patient had to be instructed to brush the gums freely, especially where they came into relation with the teeth, at least once a day, preferably twice, with a soft brush which would not scratch. The scrubbing should be carried on for some minutes with an efficient antiseptic such as a strong solution of chloride of sodium or weak chinolol. The tooth-brush should be kept quite sterilized and dried immediately after use by heavy friction on a towel. He wished to emphasize the point Mr. Colyer had made that pyorrhœa must either be cured or the teeth extracted, and perhaps Mr. Colyer could say where the dividing line was. He did not think dentists were ever justified in allowing patients to continue to swallow pus indefinitely. Patients ought to be told that pyorrhœa was, if long continued, an extremely dangerous condition, and the formation of pus must be made an end of by one means or the other.

Mr. LEWIN PAYNE said that probably members agreed with a great deal of the statements made by Mr. Colyer, but there were points on which, personally, he was bound to be at issue with him. First, with regard to the term "cure" as applied to these cases of pyorrhœa alveolaris, he considered that a comparison might be made with phthisis. If pyorrhœa could be brought into a state of quiescence in the same sense that phthisis was brought into a condition of quiescence by the treatment of the physician this quite fairly might be called "a cure." He did not think it was possible to go further, because of the liability to recurrence, when the predisposing causes were not held in check. He strongly deprecated the wholesale extraction of teeth which by treatment could be made functional and kept clean. He recalled to mind a case in which a female patient, aged 33, was condemned to have every tooth extracted and came to him for treatment in the hope that some of them might be saved. In addition to the periodontal disease she complained of constantly recurring headaches, was losing weight, and suffering from gastro-intestinal trouble. This was nine months ago and the patient had undergone local treatment accompanied by vaccines and not one tooth had been removed. The headaches and gastro-intestinal trouble had disappeared, she had gained more than a stone in weight, and her teeth were now quite firm, although X-ray examination showed that no restoration had taken place in the alveolus. On the other hand, he could quote cases in which the mouths had been made entirely edentulous and the patients had had artificial dentures inserted, but the trouble had not improved to any degree. Every dentist recognized that artificial dentures did not restore mastication to the full efficiency of Nature. It seemed to him that Mr. Colyer's experience with vaccine treatment had been extremely unfortunate. He himself had had a number of cases which he considered to have been cured, although he would not go so far as to say that every patient who came for the treatment of pyorrhœa alveolaris could be cured by vaccination. He was certain, however, that in some cases complete

extraction was detrimental to the patient, and if dentists were going to agree with Mr. Colyer in that matter they might as well drop the name of Dental Surgeon and call themselves "Extractors and Adaptors of Teeth." He would like Mr. Colyer to explain why he thought that vaccines should be used in cases of other suppurative conditions of the body and yet be absolutely ineffective in similar conditions of the mouth.

Mr. BIRT thought the conservative treatment of periodontal disease, even in its advanced stages, in certain cases was worth undertaking, if only from an experimental point of view: though he considered cases of cure by conservative treatment were sufficiently frequent to warrant that treatment being regarded as suitable in many cases and as having to that extent passed out of the experimental stage. He recalled the case of a man who was brought to his notice in the Dental Department of St. Thomas's Hospital, a case of peculiar interest because he regarded it as a successful treatment by the application of Bier's "passive congestion" as suggested by Mr. Woodruff. He first saw the patient a year ago when he had been treated for over three years by medicines for mucous colitis without any effect, indeed he had been growing steadily worse, was considerably emaciated, and had had to give up work. He was suffering very badly from periodontal disease with a very free flow of pus from around every tooth in his mouth. He had very spongy gums which bled at the slightest touch. There was a hard, dark ring of tartar round every tooth, which tartar was carefully scaled away. The periodontal membrane was stripped for a considerable distance up all the teeth, and in the left upper six-year molar was stripped up to the apex of the buccal roots. Because this tooth was so loose he feared the suction treatment might bring it out, and he therefore extracted it. The only other tooth extracted was the left upper wisdom which was carious. Before the suction treatment was commenced the patient was sent to the Dental Hospital to have this latter tooth stopped: he was there told that extraction of all his teeth was the only possible treatment and they refused to do the stopping. Accordingly this tooth was also extracted. He then made the suction apparatus and attached to it a strong vacuum pump. The gums at first bled so freely that he had to interpose a bottle between the gums and the pump to catch the blood. He taught the patient to use the apparatus himself which he did twice a day for six weeks. By that time the bleeding had almost ceased and the gums had shrunk and become more tense. The patient then used it once a day for five weeks, and at the end of that time the mouth was clean and healthy. The patient had had no treatment for the last ten months and his mouth was still in good condition. The gums were now so shrunken that the pockets were not nearly as deep as before, and the condition of the large intestine was such that he had become again a strong and healthy man and had returned to his somewhat heavy work of a printer. (This patient was in attendance and was inspected by members after the discussion.)

Mr. J. F. COLYER, in reply, said that as Mr. Bennett had attacked the statement made as to the translucent zone, and had said that was an index of the amount of scientific knowledge that had been brought to bear on the paper, it was necessary to reply somewhat in detail. His (Mr. Colyer's) idea that the translucency was due to a reaction on the part of the soft tissues was based on the fundamental principles of general pathology. Whenever a tissue was hurt, whether by trauma, toxins, or what was sometimes termed physical insults, that tissue reacted to injury, and the soft tissue of teeth reacted to injury by undergoing a certain degree of calcification. He had, therefore, the broad lines of pathology on his side, and he also had practically the whole of those who had written on the question of the translucent zone on his side also. The majority of those who had read the discussion which took place between Mr. Bennett and the late Dr. Miller would, he thought, have much hesitation in coming to the conclusion that the translucent zone was due to a calcification of the fibrils, and in no sense was due to a decalcification of the dentine. He thought Mr. Bennett's attack upon him was a little hard. A large amount of the discussion turned on pathology, but he had not come there to read a paper on the pathology of periodontal disease, having dealt with that subject very thoroughly in a book he had published. Nobody could get a grip of the pathology of periodontal disease unless he quietly studied the condition in the whole of the animal kingdom. Anyone who would take the trouble to examine a series of horses would have the whole of the question of the pathology of periodontal disease in front of him, because in the horse one met with all stages of the disease, from slight injury to the margin of the gum to the most advanced stage of suppuration. With regard to treatment, he had tried to insist upon the fact that the whole essence of the treatment was the drainage of the stagnation area. The specimens referred to by Mr. Sturridge were drawn from the Museum of the College of Surgeons and were not those of his own patients who had come to the post-mortem table. With regard to the question raised by Mr. Hopewell-Smith, he would not discuss the pathology of periodontal disease, but he agreed that instruments should be sterilized, and if he might speak as a teacher, he would say that if the dental profession understood the use of a straight probe in examining the mouth for pockets they would get a very much broader knowledge of what really existed in patients' mouths. He thought that comparatively few practitioners ever took the trouble to examine the pockets by a probe, but such a proceeding was necessary to obtain an idea of the amount of disease present. With regard to collar crowns, he had never seen one that did not cause trouble to the soft tissues, unless the collar crown happened to be above the gum margin. As to mouth-breathing, it was just a question of difference between himself and Mr. Hern. He himself considered that mouth-breathing was one of the most important factors in the production of gingivitis. He was certain that no person who breathed through his mouth, though he cleaned his teeth, was ever really free from gingivitis. This might be illustrated by a child who possibly had never cleaned its teeth, but who had the functional use of the teeth in

mastication and was a mouth-breather; the back of the mouth was clean, but the front of the mouth was dirty. This showed it was not want of friction of the tooth-brush, but the want of function leading to stagnation around the anterior tooth. The question of cure, he knew, would raise trouble. The analogy drawn by Mr. Payne between periodontal disease and phthisis was no analogy at all. The reason why a cure could not be brought about with vaccines was quite simple. Unless the pocket was cleared out round the gum, the vaccine did practically no good. Mr. Baldwin had asked what was the dividing line between extraction and treatment. The whole question turned on whether the patient had signs of general disease or not, and this was really the point he wished to bring out. He was quite convinced that if a case of periodontal disease was associated with general symptoms, as, for instance, rheumatoid arthritis, it was the duty of a dental surgeon to clear that patient's mouth of every possible source of sepsis, and the only way to do that efficiently was to take out the teeth. Mr. Payne's contention that he had seen patients rendered edentulous, yet not cured, was explained on the lines that in many cases the teeth were removed too late. The constant passage of septic matter into the patient damaged the tissues so much, with the result that when the toxic matter was removed it was too late—fibrosis followed, and probably the condition of the patient was worse than before.

Odontological Section.

February 26, 1912.

Mr. H. LLOYD WILLIAMS, President of the Section, in the Chair.

Two Cases of Hypoplasia of Enamel.

By J. G. TURNER, F.R.C.S., L.D.S.

Two children, a boy and a girl, were exhibited, showing the early stage of enamel hypoplasia. In the boy the condition was a more or less general one—i.e., it extended symmetrically round a large number of the permanent teeth, and, so far as its position was concerned, it apparently referred to somewhere about the third year of life. As a matter of fact there was a history of severe measles in the third year, and, especially on the lower teeth, a distinct band of white-coloured enamel was to be seen marking the interference with the formation of the enamel: it was the first stage of enamel hypoplasia. The enamel was full-bodied, but wanting in molecular constitution. It could not be seen so well in the boy's upper teeth, but it was to be seen extending to the canines and perhaps the first premolars.

The second case, the girl, was exhibited for the purpose of showing the localized condition. The enamel hypoplasia was in the first stage, and the condition affected the left lower permanent central, lateral, and canine. The canine had a wonderful yellow colour on it which he could not explain; the patch on the front of the lateral was less yellow, and that on the front of the incisor dull white, but both lateral and canine also showed some dull white enamel. The enamel was also full-bodied. Obviously a local cause had to be sought. The history was very distinct. At the age of 3 the temporary teeth in that position were taken out for abscess, and, later, he had extracted all the remaining temporary teeth

for sepsis, so that the permanent teeth had been interfered with in their growth by the spread of inflammation from the septic temporary teeth. As far as the tooth itself was concerned the same result, the first stage of enamel hypoplasia, was brought about, but localized. It would be seen that on the coronal half of the canine the hypoplasia spread right round—i.e., the inflammation involved the whole of the growing enamel organ. Discrete patches were very often found on one surface of a tooth only, a surface often affected being the anterior surface of the incisors, because the roots of the temporary incisors were in near approximation to that surface. The inflammatory process must spread considerably to reach to the backs of the incisor teeth.

DISCUSSION.

The PRESIDENT (Mr. H. Lloyd Williams) said he had noted the dark and pigmented patches to which Mr. Turner had referred several times, and they were very difficult to understand. He did not know whether any of the Fellows had any experience of cutting sections from such teeth. He believed that Mr. Charters-White used to say that the white patches were as like as possible to composite rock—i.e., absolutely without a plan, as the enamel prisms had lost their shapes and were simply a jumble without any definite structure.

Mr. DOWSETT asked whether Mr. Turner looked upon the cause of the isolated patches in the temporary teeth in the girl as the same as the condition in the boy. The condition of the boy he understood was developmental, but in the girl he thought the isolated patches must be post-developmental, the result of a pathological change acting upon the enamel, because that portion of the enamel would be formed before the stage of inflammation in the temporary teeth. With regard to the discoloured patches, he had actually cut sections from two upper temporary incisors with brown patches upon them, and the microscopic appearance was very much the same as the ordinary appearance of enamel prisms, but the "brown striae of Retzius" were very thick and well marked.

Mr. SIDNEY SPOKES said he had not seen the girl, but he understood from what Mr. Turner said that one cause of the trouble which he had described was abscess of a temporary tooth producing hypoplasia marks on the permanent successor. Some years ago, in a school of 800 children, he was very careful to take notes of all cases he came across where there was undoubted abscess of the temporary teeth and where the succeeding teeth, which he had the opportunity of seeing afterwards, were absolutely un-

blemished and free from any appearance of hypoplasia. That was particularly the case in bicuspid teeth where the temporary molars were commonly abscessed, and the bicuspid teeth afterwards were found to be quite free. The girl had, he thought, hypoplasia of the temporary teeth, which was distinctly more rare. Every authority that had dealt with hypoplasia was agreed upon the fact that temporary teeth were not so frequently affected as permanent teeth. With regard to the boy, he thought his lateral incisors had escaped, as they very frequently did in such cases. The general condition seen in hypoplastic front teeth was a mark on the central incisor, the tip of the canine, and the lateral incisors escaped. He was quite certain in his own mind that that was the usual experience in the ordinary well-developed cases of hypoplasia of the enamel. Mr. Turner now produced a case in which it was in its very early stage, so that some of his remarks perhaps would not hold good.

Mr. J. F. COLYER asked if Mr. Turner could explain why in that case there was a hypoplasia with the complete thickness of the enamel, while in other cases complete destruction occurred apparently of the enamel organ.

Mr. J. G. TURNER, in reply, said that he had not been able to make sections of the early stages of hypoplasia because he had never been heartless enough to extract any teeth of that kind. If anyone would send him such teeth he would be very pleased to do so. With regard to the cause of the isolated patches in the girl and the bands in the boy, they were practically identical—either circulating toxins or some interference with nutrition, the one absolutely local, the other absolutely general, affecting all the teeth, or portions of the teeth, being formed at that time. When once the enamel was formed there was no question of its being altered again. There were cases in which doubt might be raised with regard to whether the enamel had not been macerated in some way, but that only occurred when the teeth were retained in their dead state or were surrounded by purulent material. That, he believed, was not an explanation of the colour to which he referred, unless a *Staphylococcus aureus* infection were responsible for it. He rather thought that Mr. Dowsett and himself were not referring to the same point.

Mr. DOWSETT thought that the patch on the permanent teeth could not possibly be formed by an abscess on a temporary tooth because that portion of the enamel would be completely formed before the temporary tooth could have an abscess on it.

Mr. TURNER thought the question was rather the other way about, that the canine would not be completely formed till some considerable period after birth.

Mr. DOWSETT said he granted that was so with regard to the canine, but although he had not seen the child he had seen similar patches on the incisors.

Mr. TURNER, continuing, said there were patches on the two incisors and he was quite content that those were being formed before the age of 3. No

difficulty was experienced in understanding the matter if the way in which enamel is plastered on over a cusp in constantly increasing cones was borne in mind. There was also the fact that at the end of the process there might be additions of partial cones. That he had not been able to work out, but undoubtedly the whole outer layer approximately corresponded. In one of the incisor teeth of the boy two patches could be seen which were obviously formed at the same period. With regard to Mr. Sidney Spokes's objection that he examined a large number of cases and did not find the condition, he could only say that the histories were good in an astonishing number of cases if a practitioner only had sufficient material going through his hands. If he had not he could hardly expect to find them. It was possible to get not only the histories, but the actual material in situ. Personally he had models of the dead temporary tooth, the actual dead temporary tooth and the necrotic succeeding tooth in his possession. The range of injury varied from the specimen he had shown to absolute death and embraced a large number of quaint forms and monstrosities which had been described chiefly as dilaceration. There was a very good specimen showing the condition in the Museum of the Royal Dental Hospital of London in which the permanent teeth had been killed outright. With regard to the question of the complete thickness of the enamel, he presumed that depended entirely on the time at which the injury occurred and the extent of the injury. If the injury was extensive enough, then all that could be hoped for was that some enamel would be formed lower down where the growing enamel organ had just escaped. If the injury was more extensive the whole thing was killed. If the injury was not very extensive a little overlapping might be obtained, and sometimes a good enamel succeeding a bad enamel. If sections of hypoplastic teeth were taken after they were decalcified it would be found that a very thick Nasmyth's membrane appeared to be present; not a true Nasmyth's membrane, for under the microscope it showed the traces of enamel formation, in fact it showed very well that it was the organic matrix of enamel prism. It was the last despairing effort of the enamel organ to form enamel, but it had never got calcified, and remained as an acid-resisting membrana preformativa. There was every grade between absolute death and consequent want of enamel right up to fully formed but badly coloured enamel, and he thought soft enamel. White hypoplastic enamel was, he thought, softer than normal enamel.

Radiographs of a Case of Advanced Periodontal Disease.

By J. F. COLYER, M.R.C.S., L.D.S.

MR. COLYER stated that his object in showing the radiographs was to illustrate a point he endeavoured to impress upon the members at the last meeting—namely, that before an accurate idea could be obtained



FIG. 1.

Radiographs of the maxillary and mandibular incisors.

of the condition that was being treated it was necessary to have a radiograph. The patient in question was referred to him by a medical friend with a view to replacing a pin in a fixed apparatus made to keep in his lower incisors. The gum margins of the patient were just below the level of the necks of the teeth. The mouth was moderately clean, and the patient had been submitted to a prolonged course of vaccine treatment. The radiographs are shown in figs. 1 to 3.

DISCUSSION.

Mr. J. G. TURNER thought the communication was a very opportune one, because Mr. Colyer read a paper at the last meeting which he (Mr. Turner) wished to support. He took it that what Mr. Colyer meant by his paper was that there was a large amount of sepsis in the mouth which people ignored in their desire to save teeth—that cure should mean a possibility of freedom from recurrence. To secure this, every tooth must be rendered cleansible and every pocket destroyed and laid open. There were a large number of people whose health and, indeed, lives were endangered by the retention of pyorrhæic teeth. Dentists should therefore enlarge their ideas of extraction, and begin to restrict their desire for the salvation of teeth. He was constantly amazed at the amount of sepsis people were deliberately advised to carry about in their mouths, whether as the result of disbelief in the pathology which ruled in the rest of the body, or as a result of an extravagant idea of the value of tooth mastication, or merely as the result of short-sightedness and want of a good light. This was an extraordinary fact to anybody who appreciated ordinary pathology. The question was asked, "When shall we extract?" and the answer was, "When the patient cannot keep the teeth aseptic." Mr. Colyer's casual communication showed that there was too much of the spirit of compromise about which compromised with the Devil too freely. People put on fixation apparatus and thought they had cured the disease because they had fixed the teeth. As a matter of fact, they had often made the patient's condition far more perilous than it was before. They had generally hidden the disease, and the patient lived in a fool's paradise. There were very few cases where the pockets had been thoroughly laid open, because, as a rule, they had not been explored; but there were a large number of cases where bridge work and fixation work were done or crowns were put on and the patients came in reeking of pyorrhæa and showing some wonderful dentistry. This ought to be condemned everywhere. They might compromise, but the limits of compromise were fairly obvious. When the patient's resistance was good they might compromise; when the patients had been put in a cleansible condition they might compromise; but before that there was no compromise. When resistance broke down that was not the time to give an eye for a tooth. In his opinion a great many more teeth ought to be extracted than was the case at present.

Mr. D. GABELL asked Mr. Colyer whether he understood him to say there were no pockets at all round the teeth.

Mr. J. F. COLYER, in reply, said that was far from the case. The patient was said to be cured, and simply came to him to have the pin replaced. There were deep pockets round every tooth.

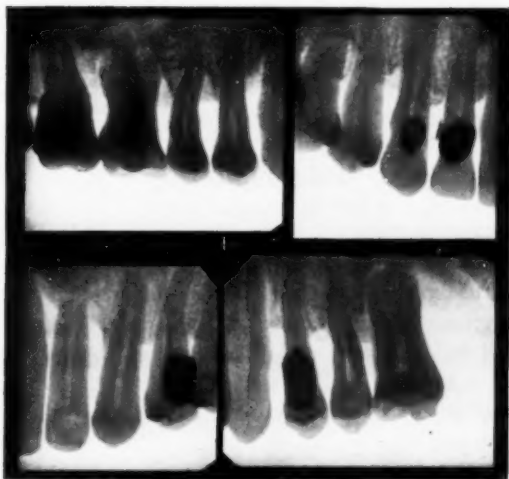


FIG. 2.

Radiographs of the maxillary premolars and molars.



FIG. 3.

Radiographs of the mandibular premolars and molars.

Some Notes on the Dates of Eruption in 4,850 Children, aged under 12.

By W. W. JAMES, F.R.C.S., L.D.S., and A. T. PITTS, M.R.C.S., L.D.S.

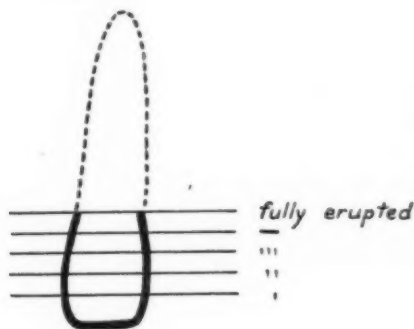
OUR investigation into the dates of eruption of teeth has been conducted at the Hospital for Sick Children, Great Ormond Street, upon all the children who have attended the Dental Department during a period of about five years. The age-limit of children attending the Hospital did not permit us to extend our investigation beyond the age of 12, when attendance automatically ceases. Nearly 7,000 new patients were examined, of whom 4,850 showed permanent teeth present or erupting, and upon which our data are based.

Method of Recording.—The method of examination was rendered constant as far as possible by one of us always making the examination of the teeth while the other recorded the results. The condition of eruption of each tooth was noted in five stages which is best illustrated by the following example:—

No. 6400. Male, aged 9 years and 4 months.

6	4"	2'''	1	1	2	4'	6"
6'''	5'	4"	3'	2	1	1'''	2'''
Hyp.							

This is a specimen case taken from our series, and illustrates the system of notation used. ' = tooth just erupted; " = less than half of crown erupted; ''' = rather more than half of crown erupted; - = almost fully erupted; whilst the absence of marks indicates complete eruption; Hyp. = hypoplastic.



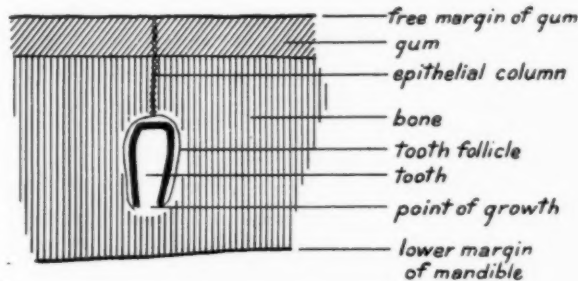
We found little difficulty in determining the class into which the teeth should be placed except with regard to complete eruption. At first it was not intended to use the - sign, but we were compelled to adopt some method of indicating that the teeth were not fully through, and so were led to make some observation on the process of eruption.

A completely erupted tooth presents the following characteristics: The crown of the tooth projects so that all the enamel is exposed except that portion covered by the free margin of the muco-periosteum (gum). The root of the tooth is firmly planted in the alveolus, which should be on a level with the neck of the tooth. The periodontal membrane is completely developed. The gum is firmly bound down to the bone, presenting a thin even margin in close contact with the tooth immediately beyond its continuation with the periodontal membrane.

The changes occurring during the period between the earliest state, when the tooth is buried deeply in the tissues and that of complete eruption, need to be considered. Much discussion has taken place concerning the nature of these changes. It would appear to us that there are two distinct factors bringing about this alteration:—

- (1) A process of advancement of the tooth in the tissues; this is generally recognized.
- (2) A process of denudation by absorption of the tissues overlying and surrounding the tooth.

With regard to the first factor, we are of the opinion that the point of eruption is determined by the presence of the epithelial columns connecting the oral epithelium with that lining the tooth-follicle. The advancement of the tooth is partly due to unequal rates of growth between the various tissues surrounding the tooth. We think it probable that the elongation of the root plays some part in advancing the tooth as represented in the following diagram:—



This is supposed to represent a lower incisor; we know growth occurs at the point marked with an arrow. As the crown is calcified it must either advance or the tissues below must be replaced. It is impossible to imagine, when we consider the length of the root, that concomitant growth of the jaw takes place to the same extent; and if X-rays of the jaw—e.g., those of Symington and Rankin—be examined, it will be seen that the base of the tooth where the root is going to be formed is so situated that it cannot be elongated in a downward direction. Another factor in the different rates of growth will appear to be the activity of the immediately supporting tissue which may be regarded as carrying the tooth to its final position, a view supported by other observers.

So far we have considered the unequal growth of tissue in a vertical plane only, but concurrently with this unequal growth also occurs in a horizontal plane. Sections made by one of us show that the epithelial column connecting the oral epithelium with the follicle undergoes degeneration centrally, and proliferation of the deeper cells of the oral epithelium takes place; with this change an unfolding occurs in the upper part, thus exposing a lower portion which in its turn undergoes a similar change. This reduces the depth of the tissue overlying the tooth which is therefore passive so far as the change is concerned. The process may be compared to the opening of a book, the hinged portion being advanced *pari passu* with the separation of the pages of the volume until it comes to occupy the same level as the free edges.

The second point that we wish to make is the process of denudation as a factor in exposing the tooth. This factor plays an important part in the final eruption of all teeth, coming into play earlier in some cases than others. The tooth which best illustrates the process is perhaps the first mandibular molar. If the first molars be examined in their earliest stage of eruption, it will be seen in the majority of cases, that although only just piercing the gum, they are in partial occlusion. There still remain ways by which room for the advancement of the tooth is possible. This space could be obtained by a closer adaptation of the occlusal surfaces; by a lengthening of the ramus of the jaw and by an advancement of the mandible; we believe all these do occur. The last factor, though not yet established is, in our opinion, of importance. Yet we do not think these factors of themselves sufficient to account for the complete eruption of the teeth by advancement, and we are of the opinion that the explanation must be sought for in the denudation of the

tooth by absorption of the tissues overlying it, a change we regard as being mainly due to the functional stimulus of mastication.

It is probable that everyone will agree that a tooth which has already perforated the gum is further exposed by the absorption of the tags of gum overlying it. We would like to point out that if this process be continued until the loose flaps of gum are removed down to the neck of the tooth, leaving the gum closely attached to the periodontal membrane with its free margin protected by the bulge of the tooth above it, the state of complete eruption is reached. The difficulty of determining the conclusion of this latter stage is considerable owing to the long period of time occupied even in healthy mouths. In unhealthy mouths, as in the case of the incisors in mouth-breathers and other conditions of impaired function, the change is much prolonged. Some cases, indeed, would appear to remain in a state of incomplete eruption almost indefinitely; this is particularly so where a condition of so-called pyorrhœa becomes established, as this affection is undoubtedly liable to occur in mouths where the absorption is incomplete.

In collecting data for this paper we came to the conclusion that it was almost impossible to draw a distinction between our last two groups—namely, the \sim and the fully erupted. Our figures represent the teeth just erupting and the total number of teeth present in the mouth; all teeth which had less than half the crown exposed being regarded as just erupting.

Before continuing with the results of our investigations it may be of interest to record our method of procedure in procuring the data. In addition to recording the stages of eruption as already described we also noted the following particulars: Carious teeth present and conditions of hypoplasia; conditions of inflammation and suppuration; glandular enlargements which were so constantly present that they were afterwards omitted; mode of feeding in infancy; state of the child's general health as recorded by the physician or surgeon. It may be stated here that the great majority of the children were sent from other departments of the hospital, in many cases whether there were dental lesions present or not. Any special abnormalities were also recorded, but cases of cleft palate and similar conditions leading to abnormal dentition are not included in our tables.

The first stage in tabulating the data was to group the cases together in periods of three months ranging from 5 to 12 years, a separate list being made of teeth erupting prior to 5 years. The teeth present, and those just erupting, were then separately recorded for each group

of three months. The number of cases in each group, and the number of teeth present, and of teeth just erupting in that group, were determined; and in order to arrive at the percentages of a particular tooth, the number present on each side of the jaw (maxilla or mandible) were added together and halved. In order to make this more clear in, for instance, the case of the first mandibular molar:—

If a = the number of cases,

If x = the number of first mandibular molars of the right side,

If y = the number of first mandibular molars of the left side,

$$\text{Percentage} = \frac{x + y}{2} \times \frac{100}{a}$$

The following tables have been compiled in this manner, and from them a series of curves have been determined:—

PERCENTAGE TABLE OF 6 | 6 (TOGETHER).

From	Age of child				Total number of teeth present		Number of teeth just erupting	
	Years	Months	Years	Months	Per cent.		Per cent.	
5 0	5	0	5	3	...	19.7	...	9.3
" 5 3	5	3	5	6	...	26.4	...	10.3
" 5 6	5	6	5	9	...	29.1	...	18.3
" 5 9	5	9	6	0	...	57.7	...	26.4
" 6 0	6	0	6	3	...	63.2	...	27.5
" 6 3	6	3	6	6	...	80.9	...	30.5
" 6 6	6	6	6	9	...	77.1	...	30.5
" 6 9	6	9	7	0	...	89.0	...	17.6
" 7 0	7	0	7	3	...	93.0	...	20.8
" 7 3	7	3	7	6	...	96.8	...	13.7
" 7 6	7	6	7	9	...	95.2	...	9.0
" 7 9	7	9	8	0	...	98.2	...	4.0
" 8 0	8	0	8	3	...	100	...	3.5
" 8 3	8	3	8	6	...	97.0	...	2.8
" 8 6	8	6	8	9	...	100	...	—

PERCENTAGE TABLE OF 6 | 6 (TOGETHER).

From	5	0	to	5	3	...	9.8	...	5.3
"	5	3	"	5	6	...	14.4	...	10.5
"	5	6	"	5	9	...	29.1	...	17.5
"	5	9	"	6	0	...	49.4	...	20.4
"	6	0	"	6	3	...	50.4	...	24.0
"	6	3	"	6	6	...	67.8	...	28.1
"	6	6	"	6	9	...	65.2	...	22.0
"	6	9	"	7	0	...	82.0	...	17.1
"	7	0	"	7	3	...	86.9	...	24.3
"	7	3	"	7	6	...	92.0	...	14.8
"	7	6	"	7	9	...	90.4	...	11.4
"	7	9	"	8	0	...	98.5	...	4.5
"	8	0	"	8	3	...	96.4	...	4.7
"	8	3	"	8	6	...	97.1	...	2.1
"	8	6	"	8	9	...	100	...	under 1.0

PERCENTAGE TABLE OF 1 | 1 (TOGETHER).

From	Age of child				Total number of teeth present			Number of teeth just erupting	
	Years	Months	to	Years	Months	Per cent.	Per cent.		
5	5	0	to	5	3	...	6.9	...	5.0
"	5	3	"	5	6	...	12.3	...	8.8
"	5	6	"	5	9	...	13.3	...	7.5
"	5	9	"	6	0	...	35.4	...	20.4
"	6	0	"	6	3	...	39.2	...	14.4
"	6	3	"	6	6	...	66.2	...	28.1
"	6	6	"	6	9	...	60.1	...	23.4
"	6	9	"	7	0	...	79.7	...	21.1
"	7	0	"	7	3	...	84.3	...	20.0
"	7	3	"	7	6	...	94.7	...	21.1
"	7	6	"	7	9	...	90.4	...	13.3
"	7	9	"	8	0	...	94.6	...	5.6
"	8	0	"	8	3	...	96.4	...	4.7
"	8	3	"	8	6	...	96.3	...	1.4
"	8	6	"	8	9	...	100	...	1.0

PERCENTAGE TABLE OF 1 | 1 (TOGETHER).

From	5	0	to	5	3
"	5	3	"	5	6	...	1.3
"	5	6	"	5	9	...	1.7
"	5	9	"	6	0	...	8.5	...	4.4
"	6	0	"	6	3	...	8.0	...	5.6
"	6	3	"	6	6	...	18.6	...	11.9
"	6	6	"	6	9	...	22.0	...	14.4
"	6	9	"	7	0	...	37.5	...	15.4
"	7	0	"	7	3	...	46.0	...	19.1
"	7	3	"	7	6	...	56.0	...	20.6
"	7	6	"	7	9	...	68.5	...	21.9
"	7	9	"	8	0	...	80.3	...	11.3
"	8	0	"	8	3	...	85.8	...	20.0
"	8	3	"	8	6	...	88.4	...	10.1
"	8	6	"	8	9	...	93.8	...	6.1
"	8	9	"	9	0	...	93.1	...	3.7
"	9	0	"	9	3	...	98.5
"	9	3	"	9	6	...	96.3
"	9	6	"	9	9	...	100

PERCENTAGE TABLE OF 2 | 2 (TOGETHER).

From	5	9	to	6	0	...	3.4	...	2.0
"	6	0	"	6	3	...	5.6	...	4.0
"	6	3	"	6	6	...	11.4	...	10.7
"	6	6	"	6	9	...	13.5	...	6.7
"	6	9	"	7	0	...	29.2	...	16.2
"	7	0	"	7	3	...	28.6	...	16.5
"	7	3	"	7	6	...	49.2	...	28.5
"	7	6	"	7	9	...	66.6	...	24.7
"	7	9	"	8	0	...	72.4	...	17.8
"	8	0	"	8	3	...	71.8	...	21.1
"	8	3	"	8	6	...	84.0	...	10.8
"	8	6	"	8	9	...	94.8	...	14.4
"	8	9	"	9	0	...	94.1	...	6.1
"	9	0	"	9	3	...	96.7	...	4.8
"	9	3	"	9	6	...	97.2	...	5.4
"	9	6	"	9	9	...	96.8	...	1.5
"	9	9	"	10	0	...	98.4	...	2.8
"	10	0	"	10	3	...	100	...	1.8

PERCENTAGE TABLE OF 2 | 2 (TOGETHER).

From	Age of child				Total number of teeth present			Number of teeth just erupted	
	Years	Months	to	Years	Months	Per cent.		Per cent.	
	6	9	to	7	0	5.4	...	3.0	
"	7	0	"	7	3	4.3	...	3.4	
"	7	3	"	7	6	10.5	...	8.4	
"	7	6	"	7	9	20.9	...	9.5	
"	7	9	"	8	0	31.5	...	18.1	
"	8	0	"	8	3	36.4	...	21.1	
"	8	3	"	8	6	48.5	...	21.7	
"	8	6	"	8	9	63.9	...	27.8	
"	8	9	"	9	0	70.8	...	20.5	
"	9	0	"	9	3	79.0	...	35.4	
"	9	3	"	9	6	81.8	...	24.5	
"	9	6	"	9	9	82.8	...	10.9	
"	9	9	"	10	0	90.0	...	11.5	
"	10	0	"	10	3	100	...	11.3	
"	10	3	"	10	6	95.0	...	7.5	
"	10	6	"	10	9	92.3	...	7.6	
"	10	9	"	11	0	96.1	...	5.1	
"	11	0	"	11	3	97.3	...	7.9	
"	11	3	"	11	6	96.0	...	1.9	
"	11	6	"	11	9	97.4	...	—	
"	11	9	"	12	0	100	...	—	

PERCENTAGE TABLE OF 3 | 3 (TOGETHER).

From	7	6	to	7	9	3.8	1.9
"	7	9	"	8	0	2.8	1.7
"	8	0	"	8	3	5.2	3.4
"	8	3	"	8	6	5.0	2.8
"	8	6	"	8	9	6.1	4.1
"	8	9	"	9	0	14.7	4.7
"	9	0	"	9	3	17.7	16.1
"	9	3	"	9	6	19.0	13.6
"	9	6	"	9	9	28.1	14.0
"	9	9	"	10	0	45.4	19.8
"	10	0	"	10	3	39.6	20.7
"	10	3	"	10	6	61.2	25.0
"	10	6	"	10	9	55.7	17.3
"	10	9	"	11	0	67.1	16.1
"	11	0	"	11	3	75.0	13.1
"	11	3	"	11	6	77.4	14.7
"	11	6	"	11	9	87.1	20.5
"	11	9	"	12	0	74.0	9.2

PERCENTAGE TABLE OF 3 | 3 (TOGETHER).

From	8	3	to	8	6	under	1.0	—
"	8	6	"	8	9	1.0	—	—
"	8	9	"	9	0	4.1	3.8	3.8
"	9	0	"	9	3	1.6	1.6	1.6
"	9	3	"	9	6	3.6	3.6	3.6
"	9	6	"	9	9	7.8	4.6	4.6
"	9	9	"	10	0	15.2	7.8	7.8
"	10	0	"	10	3	9.4	5.6	5.6
"	10	3	"	10	6	22.5	10.0	10.0
"	10	6	"	10	9	23.0	13.4	13.4
"	10	9	"	11	0	32.3	11.6	11.6
"	11	0	"	11	3	35.5	17.1	17.1
"	11	3	"	11	6	47.8	15.6	15.6
"	11	6	"	11	9	51.3	17.9	17.9
"	11	9	"	12	0	57.4	16.6	16.6

Odontological Section

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PERCENTAGE TABLE OF 4 | 4 (TOGETHER).

From	Age of child				Total number of teeth present Per cent.	Number of teeth just erupted Per cent.
	Years	Months	Years	Months		
	6	9	to	7	0	0.7
"	7	0	"	7	3	—
"	7	3	"	7	6	2.1
"	7	6	"	7	9	4.7
"	7	9	"	8	0	6.3
"	8	0	"	8	3	8.1
"	8	3	"	8	6	10.8
"	8	6	"	8	9	10.3
"	8	9	"	9	0	18.1
"	9	0	"	9	3	20.9
"	9	3	"	9	6	28.1
"	9	6	"	9	9	29.6
"	9	9	"	10	0	42.5
"	10	0	"	10	3	33.3
"	10	3	"	10	6	50.0
"	10	6	"	10	9	44.2
"	10	9	"	11	0	60.0
"	11	0	"	11	3	63.1
"	11	3	"	11	6	65.6
"	11	6	"	11	9	79.4
"	11	9	"	12	0	77.7

PERCENTAGE TABLE OF 4 | 4 (TOGETHER).

From	6	9	to	7	0	2.1	2.1
"	7	0	"	7	3	6.0	5.1
"	7	3	"	7	6	5.2	4.7
"	7	6	"	7	9	11.4	8.5
"	7	9	"	8	0	11.6	8.2
"	8	0	"	8	3	9.4	8.2
"	8	3	"	8	6	22.4	15.9
"	8	6	"	8	9	28.8	18.5
"	8	9	"	9	0	38.0	15.7
"	9	0	"	9	3	41.9	29.0
"	9	3	"	9	6	40.9	21.8
"	9	6	"	9	9	46.8	25.0
"	9	9	"	10	0	57.8	19.4
"	10	0	"	10	3	58.4	26.4
"	10	3	"	10	6	73.7	17.5
"	10	6	"	10	9	69.2	17.3
"	10	9	"	11	0	78.0	12.2
"	11	0	"	11	3	80.2	17.1
"	11	3	"	11	6	86.2	21.5
"	11	6	"	11	9	84.6	7.6
"	11	9	"	12	0	88.8	11.1

PERCENTAGE TABLE OF 5 | 5 (TOGETHER).

From	7	6	to	7	9	1.9	1.9
"	7	9	"	8	0	2.2	1.7
"	8	0	"	8	3	2.2	—
"	8	3	"	8	6	5.0	2.1
"	8	6	"	8	9	4.1	3.0
"	8	9	"	9	0	8.8	3.1
"	9	0	"	9	3	6.4	1.6
"	9	3	"	9	6	10.0	5.4
"	9	6	"	9	9	18.7	9.3
"	9	9	"	10	0	21.9	9.0
"	10	0	"	10	3	24.5	9.4
"	10	3	"	10	6	26.2	12.5
"	10	6	"	10	9	38.4	9.6
"	10	9	"	11	0	34.7	9.0
"	11	0	"	11	3	38.1	10.5
"	11	3	"	11	6	44.1	6.8
"	11	6	"	11	9	48.7	5.1
"	11	9	"	12	0	61.1	5.5

PERCENTAGE TABLE OF 5 | 5 (TOGETHER).

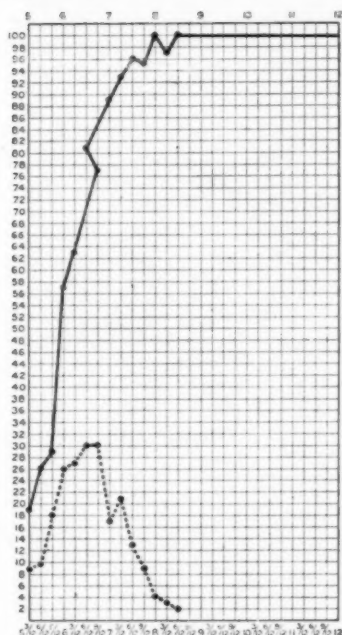
From	Age of child				Total number of teeth present		Number of teeth just erupted	
	Years	Months	Years	Months	Per cent.		Per cent.	
7	7	3	to	7	6	1.0	1.0	1.0
"	7	6	"	7	9	2.8	1.9	1.9
"	7	9	"	8	0	3.9	3.4	3.4
"	8	0	"	8	3	2.3	2.3	2.3
"	8	3	"	8	6	7.1	6.5	6.5
"	8	6	"	8	9	10.3	6.5	6.5
"	8	9	"	9	0	17.8	7.1	7.1
"	9	0	"	9	3	19.3	15.3	15.3
"	9	3	"	9	6	18.1	11.8	11.8
"	9	6	"	9	9	25.0	12.5	12.5
"	9	9	"	10	0	32.6	9.9	9.9
"	10	0	"	10	3	41.5	16.9	16.9
"	10	3	"	10	6	47.5	12.5	12.5
"	10	6	"	10	9	38.4	9.5	9.5
"	10	9	"	11	0	52.9	9.6	9.6
"	11	0	"	11	3	59.2	13.1	13.1
"	11	3	"	11	6	67.6	10.7	10.7
"	11	6	"	11	9	64.1	12.8	12.8
"	11	9	"	12	0	74.0	3.7	3.7

PERCENTAGE TABLE OF 7 | 7 (TOGETHER).

From	9	6	to	9	9	4.6	4.6
"	9	9	"	10	0	9.4	4.9
"	10	0	"	10	3	11.3	7.5
"	10	3	"	10	6	12.5	11.2
"	10	6	"	10	9	11.1	3.8
"	10	9	"	11	0	28.3	11.6
"	11	0	"	11	3	32.8	15.7
"	11	3	"	11	6	40.1	19.6
"	11	6	"	11	9	48.7	30.5
"	11	9	"	12	0	57.4	12.9

PERCENTAGE TABLE OF 7 | 7 (TOGETHER).

From	9	9	to	10	0	4.1	1.6
"	10	0	"	10	3	3.7	—
"	10	3	"	10	6	1.0	1.2
"	10	6	"	10	9	5.7	—
"	10	9	"	11	0	16.7	8.3
"	11	0	"	11	3	15.7	7.8
"	11	3	"	11	6	24.5	9.8
"	11	6	"	11	9	35.8	17.9
"	11	9	"	12	0	44.4	9.2

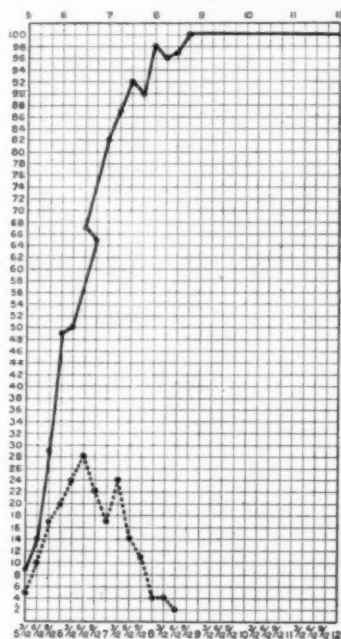


— = teeth present. = teeth just erupting.

Lower First Molars (6/6) not included in Chart.

Age	
4 yrs.	{ two 6/6 one 6/6 }
4 yrs. 1 mos.	one 6/6
4 yrs. 4 mos.	{ one 6/6 one 6/6 }
4 yrs. 6 mos.	{ two 6/6 two 6/6 }
4 yrs. 8 mos.	one 6/6
4 yrs. 9 mos.	{ one 6/6 one 6/6 }
4 yrs. 10 mos.	{ two 6/6 two 6/6 }
4 yrs. 11 mos.	{ two 6/6 one 6/6 }

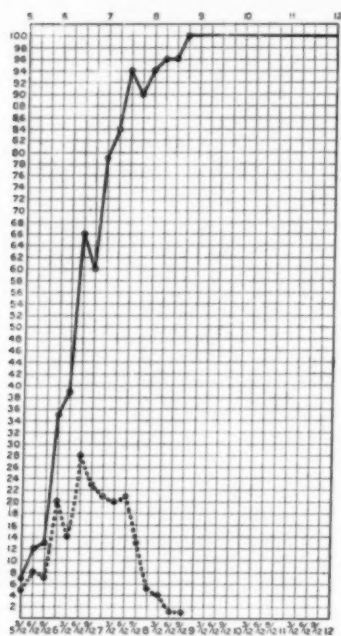
6/6 together.



Upper First Molars (6/6) not included in Chart.

Age	
4 yrs.	{ one 6/6 one 6/6 }
4 yrs. 6 mos.	two 6/6

6/6 together.



Lower Central Incisors ($\bar{I} \mid \bar{i}$) not included in Chart.

Age

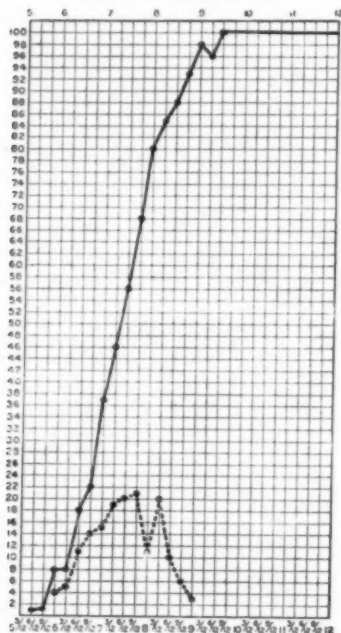
4 yrs. 6 mos. one $\bar{I} \mid$

4 yrs. 9 mos. one $\bar{I} \mid$

4 yrs. 10 mos. {one $\bar{I} \mid$
one $\bar{i} \mid$ }

$\bar{I} \mid \bar{i}$ together.

— = teeth present. . . . = teeth just erupting.

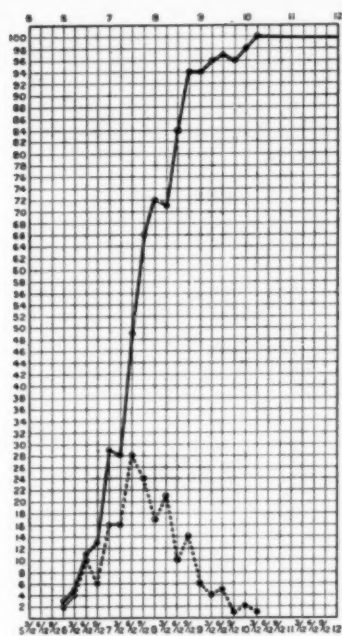


Upper Central Incisors ($I \mid i$) not included in Chart.

Age

5 yrs. to 5 yrs. 3 mos. one $I \mid$

$I \mid i$ together.



Lower Lateral Incisors ($\overline{2} \mid \underline{2}$) not included in Chart.

Age

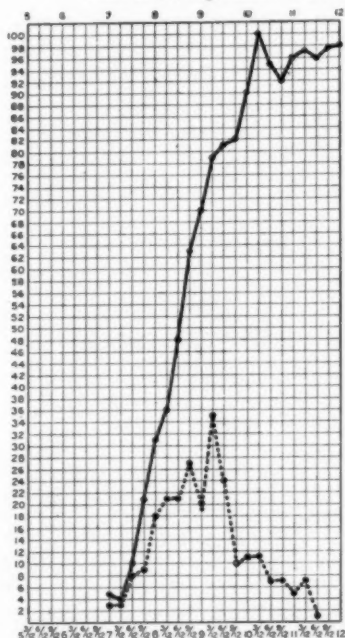
5 yrs. to 5 yrs. 3 mos. one $\overline{2}$

5 yrs. 3 mos. to 5 yrs. 6 mos. (one $\overline{2}$
two $\mid \underline{2}$)

5 yrs. 6 mos. to 5 yrs. 9 mos. (two $\overline{2}$
two $\mid \underline{2}$)

$\overline{2} \mid \underline{2}$ together.

— = teeth present. . . . = teeth just erupting.



Upper Lateral Incisors ($\overline{2} \mid \underline{2}$) not included in Chart.

Age

5 yrs. to 5 yrs. 3 mos. one $\overline{2}$

5 yrs. 3 mos. to 5 yrs. 6 mos. two $\mid \underline{2}$

5 yrs. 6 mos. to 5 yrs. 9 mos. (one $\overline{2}$
two $\mid \underline{2}$)

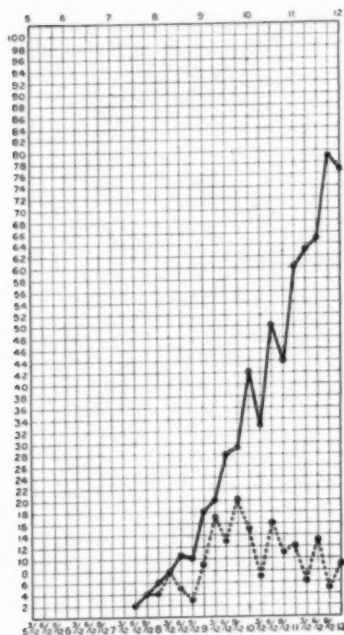
5 yrs. 9 mos. to 6 yrs. (one $\overline{2}$
one $\mid \underline{2}$)

6 yrs. to 6 yrs. 3 mos. (one $\overline{2}$
one $\mid \underline{2}$)

6 yrs. 3 mos. to 6 yrs. 6 mos. (one $\overline{2}$
one $\mid \underline{2}$)

6 yrs. 6 mos. to 6 yrs. 9 mos. (two $\overline{2}$
one $\mid \underline{2}$)

$\overline{2} \mid \underline{2}$ together.



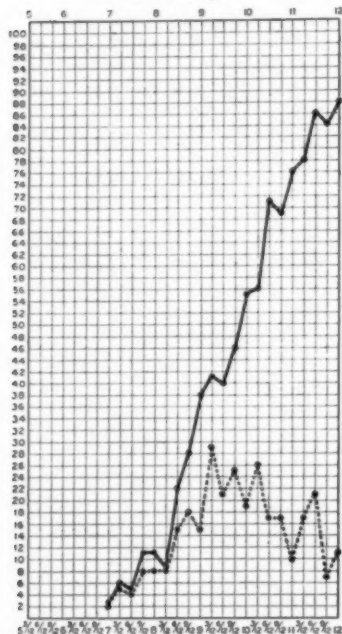
— = teeth present.

- - - = teeth just erupting.

Lower premolars (4 | 4) not included in Chart
(15 teeth).

Age

5 yrs. 6 mos. to 5 yrs. 9 mos. $\overline{4}$
 No history of $\overline{4}$
 5 yrs. 9 mos. to 6 yrs. $\overline{4}$
 { two $\overline{4}$ }
 { two | $\overline{4}$ }
 6 yrs. 3 mos. to 6 yrs. 6 mos. $\overline{4}$
 Hypoplastic
 6 yrs. 6 mos. to 6 yrs. 9 mos. $\overline{4}$
 Hypoplastic
 6 yrs. 9 mos. to 7 yrs. { three $\overline{4}$ }
 { four | $\overline{4}$ }
 7 yrs. to 7 yrs. 3 mos. $\overline{4}$

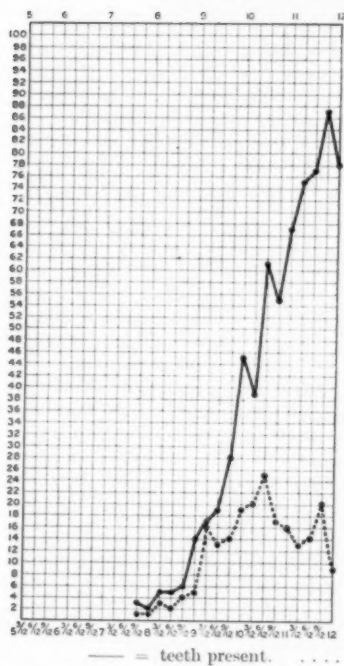
 $\overline{4}$ | $\overline{4}$ together.

Upper First Premolars (4 | 4) not included in
Chart.

Age.

5 yrs. to 5 yrs. 3 mos. one $\overline{4}$ (D)
 5 yrs. 3 mos. to 5 yrs. 6 mos. one | $\overline{4}$
 5 yrs. 9 mos. to 6 yrs. { one $\overline{4}$ }
 { two | $\overline{4}$ }
 6 yrs. to 6 yrs. 3 mos. { two | $\overline{4}$ }
 { Hypoplastic (one) }
 one $\overline{4}$ |
 6 yrs. 6 mos. to 6 yrs. 9 mos. { one $\overline{4}$ }
 { one | $\overline{4}$ }

 $\overline{4}$ | $\overline{4}$ together.



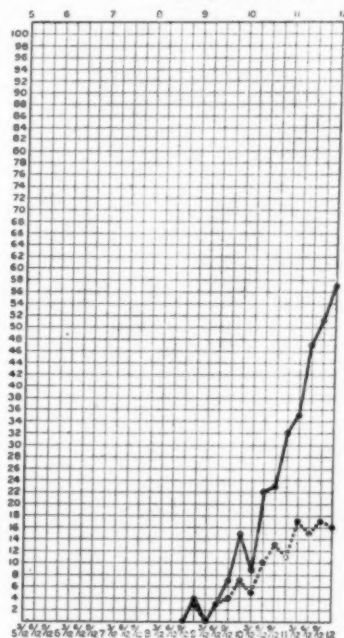
Lower Canines (3 | 3) not included in Chart.

Age.

6 yrs. 9 mos. to 7 yrs. { one 3 |

7 yrs. 3 mos. to 7 yrs. 6 mos. { one 3 |

3 | 3 together.



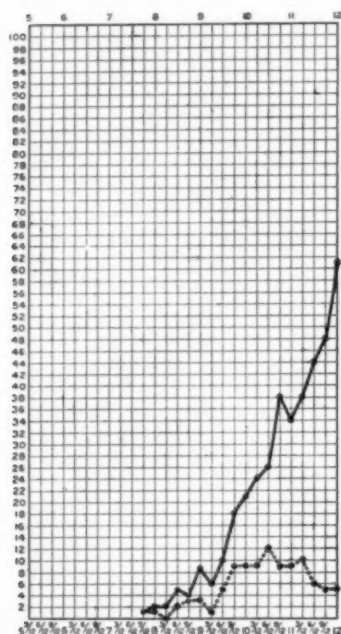
Upper Canines (3 | 3) not included in Chart.

Age.

6 yrs. 3 mos. to 6 yrs. 6 mos. { two 3 |

6 yrs. 6 mos. to 6 yrs. 9 mos. { one 3 |

3 | 3 together.



Lower Second Premolars ($\overline{5}|\overline{5}$) not included in Chart.

Age

5 yrs. 3 mos. to 5 yrs. 6 mos. one $\overline{5}$ Hypoplastic

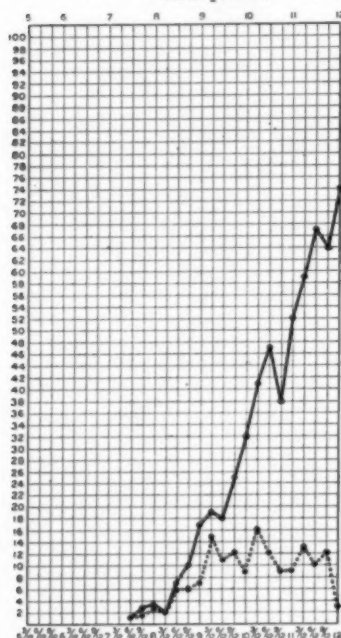
5 yrs. 9 mos. to 6 yrs. one $\overline{5}$

6 yrs. 9 mos. to 7 yrs. $\left\{ \begin{array}{l} \text{six } \overline{5} \\ \text{Hypoplastic (3)} \\ \text{three } \overline{5} \end{array} \right.$

7 yrs. 3 mos. to 7 yrs. 6 mos. $\left\{ \begin{array}{l} \text{two } \overline{5} \\ \text{one } \overline{5} \\ \text{Hypoplastic} \end{array} \right.$

$\overline{5}|\overline{5}$ together.

— = teeth present. . . . = teeth just erupting.



Upper Second Premolars ($\overline{5}|\overline{5}$) not included in Chart.

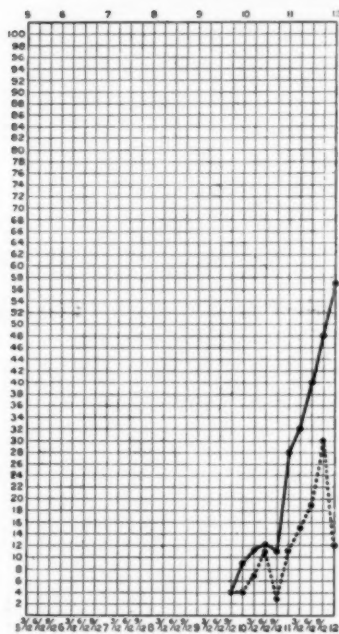
Age

6 yrs. to 6 yrs. 3 mos. $\left\{ \begin{array}{l} \text{one } \overline{5} \\ \text{one } \overline{5} \end{array} \right.$

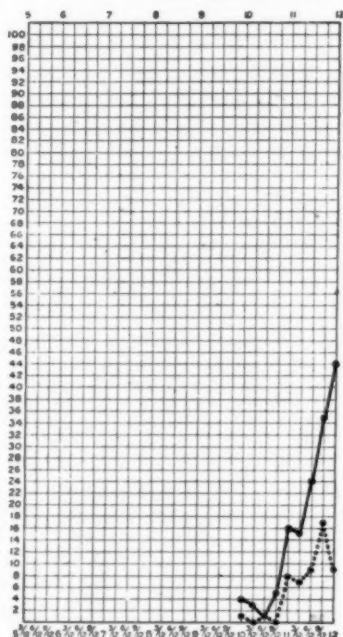
6 yrs. 3 mos. to 6 yrs. 6 mos. one $\overline{5}$

6 yrs. 7 mos. to 7 yrs. $\left\{ \begin{array}{l} \text{one } \overline{5} \\ \text{one } \overline{5} \end{array} \right.$

$\overline{5}|\overline{5}$



— = teeth present. . . . = teeth just erupting.



Lower Second Molars (7 | 7) not included in Chart.

490

8 yrs. 9 mon. to 9 yrs.	{ three 7
	{ three 7

9 yrs. to 9 yfs. 8 mos.

{ two $\overline{7}$ |
one | $\overline{7}$

9 yrs. 3 mos. to 9 yrs. 6 mos. $\left\{ \begin{array}{l} \text{two } \overline{7} \\ \text{two } \overline{7} \end{array} \right.$

7 | 7 together.

Upper Second Molars (7 | 7) not included in Chart.

Algo

9 yrs. 6 mos. to 9 yrs. 7 mos. one | 7

7 | 7 together.

It is almost unnecessary to comment on the charts, as they speak for themselves. The earliest cases of eruption occurred at the age of 4; in one $\frac{6''}{6''}$ was present, in the other $\frac{6''}{6''} \mid \frac{6''}{6''}$. The latter case is of interest, as at 4 years 6 months $\frac{1''}{1''}$ appeared, and at 5 years 1 month $\frac{1''}{1''} \mid \frac{1''}{1''}$ were present. Sixteen cases of eruption of the first molars before the age of 5 were observed; in only one case were all four molars present; of the others, in only one was a maxillary molar present. Two of these cases are of considerable interest, as the children were attending the hospital for severe rickets. In one case $\frac{6'}{1'}$, in the other $\frac{6''}{6''}$ were present.

This proportion of two cases with rickets out of sixteen cases of eruption before the age of 5 is significant, and we would like to state that, although the view has come to be generally accepted that "rickets retards" eruption, while true of the temporary dentition, is not borne out by our experience of the permanent series. We would admit that it causes variation.

The cases of early eruption, which are not included in the charts, have been placed by the side of the chart of each respective group. Comment is therefore unnecessary.

In considering the various teeth, the following points are of interest:—

6 | 6.—The curve of the teeth present shows a marked ascent from 5 years 3 months to 7 years 6 months. The maximum of teeth just erupting being at 6 years 6 months (30 per cent.).

6 | 6.—The curve of teeth present shows a marked ascent from 5 years 3 months to 7 years 6 months. The maximum of teeth just erupting being at 6 years 6 months (28 per cent.).

Although these statements make the mandibular and maxillary molars appear almost the same, if the curves be examined double the number of the former are present at 5 years 3 months, and 100 per cent. is reached practically nine months sooner.

1 | 1.—The curve of teeth present ascends markedly from 5 years 9 months to 7 years 6 months. The maximum of teeth just erupting is reached at 6 years 6 months (28 per cent.).

1 | 1.—The curve of teeth present ascends markedly from 6 years 3 months to 9 years. The maximum of teeth just erupting is reached at 7 years 9 months (21 per cent.).

The mandibular teeth again precede those of the maxilla.

2 | 2.—The curve of teeth present ascends markedly from 6 years to 8 years 9 months. The maximum of teeth just erupting is reached at 7 years 6 months (28 per cent.).

2 | 2.—The curve of teeth present ascends markedly from 7 years 3 months to 10 years. The maximum of teeth just erupting is reached at 9 years 3 months (35 per cent.).

The difference between the mandibular and maxillary teeth is here very considerable.

4 | 4.—The curve of teeth present ascends markedly, but with considerable irregularity, from 8 years 9 months to 11 years 9 months. The maximum of teeth just erupting is at 9 years 9 months (20 per cent.).

4 | 4.—The curve of teeth present ascends markedly, also with considerable irregularity, from 8 years 3 months to 11 years 6 months. The maximum of teeth just erupting is at 9 years 3 months (29 per cent.).

The maxillary teeth precede those of the mandible by about six months. The great irregularity of the curves is of interest and covers a long period. Our charts are imperfect for these teeth, as both curves in each case continue beyond the age of 12; prior to this age in neither case are 90 per cent. of the teeth present.

5 | 5.—The curve of the teeth present ascends markedly from 9 years 3 months to 12 years, when only 61 per cent. of the teeth are present. The maximum of teeth just erupting is at 10 years 6 months (12 per cent.); the curve forms a plateau from 9 years 9 months to 11 years 3 months.

5 | 5.—The curve of the teeth present ascends markedly from 8 years 3 months to 12 years, when only 74 per cent. of the teeth are present. The maximum of teeth just erupting is at 10 years 3 months (16 per cent.).

The maxillary teeth precede those of the mandible by about six months. It is of note that the curve of the second premolars is more symmetrical than that of the first in both teeth present and those just erupting.

3 | 3.—The curve of teeth present ascends markedly from 8 years 9 months to 11 years 9 months, when 87 per cent. were present. The maximum period of teeth just erupting is 10 years 6 months (25 per cent.).

3 | 3.—The curve of teeth present ascends markedly from 9 years 3 months to 12 years, when 57 per cent. were present. The maximum period of teeth just erupting occurs at 11 years 3 months and 11 years 9 months (17 per cent.).

The mandibular precede the maxillary by about a year. In both cases more than 50 per cent. of the teeth are present, and therefore the maximum points of teeth just erupting has probably been reached, although the curve is incomplete.

7 | 7.—The curve of teeth present ascends markedly from 10 years 9 months to 12 years (57 per cent.). The maximum period of teeth just erupting is 11 years 9 months (30 per cent.).

7 | 7.—The curve of teeth present ascends markedly from 10 years 6 months to 12 years (44 per cent.). The maximum period of teeth just erupting is 11 years 9 months (17 per cent.).

The mandibular teeth commence eruption a little earlier, but on examination of the curves would appear to be about three months early. These curves are, of course, imperfect.

The following table has been compiled from the charts and may roughly be taken as the average date at which the teeth appear:—

Years Months					
At	6	0	over 50 per cent. of the	6	6 were present
"	6	3	"	6	6 "
"	6	6	"	1	1 "
"	7	6	"	1	1 " } For 1 1 100 per cent. is reached
"	7	6	"	2	2 " } six months earlier than 2 2
"	8	9	"	2	2 "
"	10	0	"	4	4 "
"	10	6	"	4	4 " } 100 per cent. is not reached in
"	10	6	"	3	3 " } either case
"	11	0	"	5	5 "
"	11	9	"	3	3 "
"	12	0	"	5	5 " } 5 5 commence earlier and show
"	12	0	"	7	7 " } a larger proportion, although
After	12	0	"	7	7 " } 100 per cent. not reached
(would probably be 12 years 6 months)					

In conclusion, we realize that data based upon so comparatively small a number of cases as 4,850 is open to criticism, and also that the age limit of 12 years somewhat reduces the value of our observations; yet we believe our results have been obtained with sufficient care to render them of some use in determining rather more precisely the relative dates of eruption of the permanent teeth.

DISCUSSION.

The PRESIDENT (Mr. H. Lloyd Williams) said the paper was a very interesting one, and gave the result of years of work and very careful observation. Although the tables given by the authors supported the old formula that most students learned and that were given in the text-books generally, there were some variations which were quite surprising.

Mr. J. F. COLVER, after thanking the authors for their very excellent piece of work, said he did not intend to criticize the paper harshly, but with a view to asking them to work out a few more points in order that it might be possible to get nearer the truth. What he wished particularly to point out was that the authors' statistics were taken from sick children, which must go a long way towards invalidating the value of their results. He was perfectly certain that if the statistics were worked out for normal children, different results would be obtained from those shown. He had been very much interested in the question of glandular enlargements, to which the authors had referred. The question was simply a personal one, and it would be very interesting if by some means or other they could arrive at some idea of what a gland really was. It would be of interest if the authors would state whether in compiling their statistics they had made a note of whether there was an early extraction of teeth, because the early extraction of a deciduous molar would cause the early eruption of a permanent molar, and the early extraction of deciduous teeth expedited the eruption of premolars. Another point which might be worked out was the question of the difference of eruption in the various social states. Another point to consider was the variations of time of eruption between the different races; there was a difference between the Jews and the Gentiles, and he would like the authors to work out the time of eruption in the long-headed and the broad-headed people.

Mr. SIDNEY SPOKES desired to emphasize the great use the investigation of the authors would be. As births were now registered, the same question did not arise as arose in olden days when the age of children was not sufficiently well authenticated. Under the Childrens Employment Act of 1893 and the Criminal Law Amendment Act of 1895 it became very important indeed to know the ages of young children. At a meeting of the old Odontological Society in 1883, Mr. Smith Turner exhibited the jaw of the girl who was found murdered in the Goswell Road, and endeavoured to obtain the opinion of the members as to the age of the individual. Although registration was now carried out, some cases still arose when it was most important that all the information as to the condition of teeth, the state of the eruption, and so on, should be made known. Certain cases also arose where registration returns

were not available. For instance, the law presumed that a child not over the age of 7 was incapable of committing an indictable offence, and that was a very important medico-legal point. Also if a child was not over 14 it was not permissible to punish it unless direct malice could be shown. There were all manners of questions that were very interesting from that point of view on which the paper threw some light. The work the authors were doing was extremely valuable, quite apart from any of the anatomical points of interest that came home to the various members. Personally he had worked out certain figures which related to people in a different class of life from those dealt with by the authors. He took very careful notes of the eruption of the permanent teeth of over 1,100 boys in a big public school, the figures extending over several years. He had therefore followed with a great deal of interest the charts shown by the authors, and found that in some points they corroborated his own figures, for instance, with regard to the lower canines. The authors' work would, he thought, afford a very important basis upon which future investigations would be conducted.

Mr. J. G. TURNER said he desired to refer to the point that Mr. Colyer had already raised, namely, that the authors' figures dealt with sick children, and that he doubted whether the results would be anything like those obtained with healthy children. One was accustomed to immense variations in all teeth, but he was inclined to think from the impression he had gathered of healthy children that their eruption would prove to be later than shown by the authors. The change of the premolars and canines was often quite a late thing. It was just as if the children began to get old later than children under other conditions. As usual, they were up against sepsis. The temporary teeth were destroyed, and that entirely upset the eruption of the premolars. If a temporary molar went too soon on account of pulp pain without surrounding sepsis, the bone was not softened, and there was no early eruption, but on the contrary a tendency to a locking in of the premolars on account of the movements of the remaining teeth, and so a later eruption. On the other hand, if the teeth had been taken out for sepsis, the bone would soften, and the succeeding teeth would erupt early. These processes would occur very largely among those children. It was not a question of one or two out of ten: it was a question of nine out of ten or ten out of ten, who might be expected to have something wrong with the temporary teeth. Again, if the first permanent molar was taken out, the second permanent molar would be expedited, especially the lower second molar, because it was unlocked. The accident that needed the extraction was so common that he was afraid they were not dealing in 50 per cent. of the cases with children who might be called fairly normal. He would like to ask the authors whether they had a note of that factor in comparing the value of the statistics? It would be more valuable where the normal or the nearly normal individuals were compared with the normal. He congratulated the authors on the results of their sustained effort, which would always be there to help investigation.

Mr. W. W. JAMES, in reply, said there were several other tables that the authors could have compared their tables with, but they thought it better not to do so because they were on somewhat different lines. The chief importance of the charts was that they gave a range of periods; they did not fix one to any particular date. Mr. Colyer and Mr. Turner referred to the question that the statistics related to unhealthy children. As a matter of fact, the children that visited the Dental Department of the Hospital for Sick Children were all outpatients and really healthy, and if any abnormal cases were seen they were practically excluded; for instance, cases such as cleft palate, of which there were a large number. A number of the children had perfect dentitions, some of them without any caries in the mouth. A great many of them were sent on from the throat department, where some of the surgeons would not treat the patients until they had seen the dentist. It was true that there was a great deal of sepsis and that a number of temporary molars were constantly removed. With regard to its effect on the permanent series of premolars, it was interesting to note that the dates given in the tables were later than the ones usually given. How far it was affected by the sepsis he did not know. With regard to the question of the illnesses the children had, those points were noted in the books, and it was possible to work out to some extent the glandular enlargements. Very careful records were kept of all the glandular enlargements. It was possible to tell with one's eyes shut whether one had a patient with the carious teeth removed or not. In about half of the cases there was very little change, but where the glands were enlarged and definitely soft it was often possible to find them contracted down to hard nodules. Personally he preferred to examine them and feel how soft or hard they were so far as the condition of activity was concerned rather than their being in an elevated condition so that they could be seen. With regard to the question of the effect of early extraction, all the cases were practically new cases. The children were all told to come back in six months so that it was possible to examine the changes that had gone on in the mouth, but the tables referred to were made up from new cases entirely. He would leave the question of the difference between the long-headed and the broad-headed people to be worked out by Mr. Colyer. He was very interested to hear of the statistics to which Mr. Sidney Spokes had referred, and it would be very interesting if some tables could be prepared from them. Mr. Turner had referred to the septic months that were commonly met with in children. If one attempted to work out statistics from what might be called the dentally normal they were really working on the dentally abnormal, because he was not sure that the mouth with a perfect temporary dentition could be regarded as normal at the present time.

**Demonstration on the Formation of Ions and their Application
in the Treatment of Periodontal Membrane.**

By ERNEST STURRIDGE, L.D.S.

ABOUT fourteen years ago I began a number of experiments with the electric current to ascertain its action on drugs when applied to periodontal membrane. The phenomenon of cataphoresis as explained by Morton, of New York, and others was uppermost in my mind, the driving of drugs *en masse* into the tissues being the main object.

I met with a certain amount of success with this method, but I also had many failures. The successes I recorded were sufficient encouragement for me to continue on the lines I had started, but gradually I became convinced that the amount of current strength possible to be used on the tissues of the mouth was insufficient to perform cataphoresis in an effective manner. I began to think that it was probable that the good results I had obtained were derived from ions and not by cataphoresis, consequently I directed my attention solely to drugs from which ions are readily formed. I recorded their action on the tissues and in this way gradually obtained a comparative list of the action of ions obtained from certain metals and alkaloids which are produced at the positive electrode, and others, like iodine, which is produced at the negative electrode.

In order to appreciate the action of ions it is necessary to understand something about their formation. The theory of ions is not difficult to understand; of late years many experiments have been performed by eminent workers in electro-therapeutics which demonstrate conclusively the formation and migrations of ions. When an electric current is passed through a conducting body or electrolyte the conductivity depends on the amount and quality of good conductor atoms contained in it; for example, pure water is a poor conductor of current, but if water contains sodium chloride (NaCl) or zinc chloride (ZnCl) in solution the liquor becomes a good conductor, that is, the atoms NaCl and ZnCl readily receive the charges of electricity and conduct them. These atoms are the ions which remain in the water in no regular formation and with no particular destiny, but directly a current is passed through the electrolyte containing them a great change takes place; the atoms become charged

with electricity and split up into their elements—certain ions become charged with positive electricity and others with negative electricity. Those which are positively charged move in the direction of the negative pole while those which are negatively charged migrate in the direction of the positive pole. In the case of zinc chloride in solution, when a current is passed through it the Zn ions become charged with positive electricity, disassociate from the Cl ions, and migrate towards the negative electrode, while the Cl ions become negatively charged and migrate towards the positive electrode.

This disassociation and migration of ions by the action of the current is the conception on which ionic medication is based. The liquid or compound through which the current passes is an electrolyte and consequently a conductor, but it is a different kind of conductor to a metal, such as copper wire. In conducting current through an electrolyte a chemical change takes place, as shown already by the splitting up of the ZnCl atoms into Zn ions and Cl ions. We must regard the body as an electrolyte and chemical changes take place when the current is passed through it.

One of the strong features in favour of ionization is the small amount of current strength required to form ions, and the rapidity with which they are formed. A convincing ocular demonstration of the formation and migration of ions was carried out a few years ago by Dr. Lewis Jones in another branch of this Society when he showed conclusively that ferrous ions and copper ions migrated from soluble electrodes and penetrated many layers of filter paper, and then through many folds of parchment paper. These experiments I have repeated myself with this little apparatus I have here, but I find them more difficult and complicated than the experiment I propose to carry out now. I am, however, indebted to Dr. Lewis Jones for the idea of mixing chemicals with the electrolyte in order to colour the ions.

I have here two glass tubes each 6 cm. long and 1 cm. in diameter, open at both ends, these tubes are filled with coagulated albumen. In one tube the albumen has been mixed with a trace of ferricyanide of potassium, the other contains pure albumen. The tubes are placed side by side standing on the small platform which has a platinum electrode connected by wire to the thumbscrew, to which is attached the negative lead wire; the other ends are in contact with a similar electrode which is connected with the other thumbscrew, to which is attached the positive lead wire. The albumen is the electrolyte, which being white, readily shows the movement of ions as they take place. Two lengths

of iron wire each 2 cm. long and 1 mm. thick are placed one on each end of the glass tube containing the mixture of albumen and ferricyanide of potassium, passing along the side of the glass so that they are readily seen, the ends of the wire are bent over the sides of the glass and are in contact with the platinum electrodes. A similar arrangement is carried out with copper wire in the other glass tube which contains pure albumen.

The reason for mixing ferricyanide of potassium with the albumen in the tube in which is placed the iron wires is that ferrous ions are invisible, but when brought in contact with ferricyanide of potassium Prussian blue is formed. Iron and copper are both soluble electrodes, and when a current of about 5 ma. is passed you can see ferrous ions and copper ions migrate from the surfaces of the metals, the ferrous ions staining the albumen a Prussian blue and the copper ions a light green; this takes place at the positive pole. At the negative pole no change takes place except the formation of hydrogen gas. I would draw your attention particularly to the rapidity with which the ions are formed and the depth of penetration.

It has been conclusively shown by many workers in electro-therapeutics that ions of zinc, copper, silver, and iodine have strong antiseptic properties; the principal advantage they possess over ordinary methods of applying them in treatment is that with their electrical charges passing through an electrolyte like the body the ions penetrate the cells of the tissues and (probably on account of a certain amount of coagulation of albumen) are not readily affected by absorption into the general circulation in the same way as drugs which are hypodermically injected; the only question is the depth to which penetration takes place; this seems to me to depend on the amount of current strength which is possible and the kind of tissue which is under treatment; periodontal membrane, for example, will permit of greater penetration than the epidermis.

In medical electro-therapeutics ions of zinc are successfully used in the treatment of such affections as rodent ulcer, lupus, pus-yielding sinuses, &c. In dental practice there are many difficult problems yet unsolved, the most difficult of these are the ones in which ionization, to my mind, is a step in advance of other methods placed at our disposal. I will briefly mention a few of these:—

Periodontitis from septic root: If an electrode is introduced into the root canal and a solution of 3 per cent. zinc chloride applied with a current strength of 3 or 4 ma., ions of zinc are freely formed and

migrate, not only through the foramen, but into the structure of the canal walls; these ions are highly antiseptic and most tolerated by the periodontal membrane.

Chronic alveolar abscess with fistulous opening on the gums: If the root is treated in the same manner with zinc ions and then the fistulous tract probed to its origin with a copper probe and a platinum electrode connected to this in situ, with a small current strength of 2 to 4 ma. the soluble copper will emit copper ions into the septic tract. I have often treated these sinuses which have been long standing, and have known them to heal completely after one or two treatments of ten minutes' duration.

Pyorrhœa alveolaris: This is the principal use to which I put ionic medication, and there are many forms of gingivitis for which it is admirably adapted. The subject of treatment of pyorrhœa by ionization is one which will require more time than is at my disposal to-night for the casual communication; there are, however, a few points of interest which I am frequently questioned about, which I will briefly refer to.

The drugs I have found most efficacious are zinc chloride 3 per cent. solution, cuperol 2 per cent., and argyrol 5 per cent., from which ions of zinc, copper, and silver, are formed at the positive pole, and iodine from which ions are formed at the negative pole.

The current strength necessary to form ions is low, 0.5 ma. is perhaps the lowest, but 2 or 3 ma. is sufficient, and this amount is readily tolerated by most patients. The most I have known a patient to take is 15 ma. The stronger the current, the deeper the penetration, and the more rapid the effect of the treatment. It is not desirable to apply the opposite element close to the site of ionization. On the face, for instance, if the electrode is held in the hand contact is just as effective and more comfortable to the patient.

The point I would make in favour of ionization in the treatment of pyorrhœa and other affections of the periodontal membrane is one which may appeal to many, that is, that no matter how careful and complete instrumentation may be, the application of antiseptics by the ordinary methods of syringing, irrigation, or wiping out pockets, is quite inadequate for effective and lasting treatment, because the micro-organisms are not merely on the surface, but penetrate deep into the tissues, and are even to be found in the circulation by ionic medication. Ions migrate through the very protoplasm of cells, and micro-organisms which would not be otherwise reached are antiseptically treated.

I am convinced that far too little attention is paid to the part which micro-organisms play in the ravages of pyorrhœa, and that many ardent and skilful workers fall just short of success in treatment, because sterilization is imperfectly carried out, that re-infection occurs before the tissues can recover. Certainly irrigation, syringing, spraying, and the like, are but preliminary steps to perfect sterilization.

I have no hesitation in asserting, in spite of recent utterances to the contrary by would-be eminent authorities on the subject, that any ordinary case of pyorrhœa can be cured by ionization in conjunction with proper attention to the many other details which constitute effective treatment of this troublesome disease.

Odontological Section.

March 25, 1912.

Mr. H. LLOYD WILLIAMS, President of the Section, in the Chair.

A Case of General Exostosis of all the Maxillary Teeth.

By ERNEST B. DOWSETT, M.R.C.S., L.D.S.

THE case I am about to describe, as far as I am able, is one of productive periodontitis or exostosis involving all the teeth in the maxilla. The patient was not one of my own, and was lost sight of before a few points could be elucidated; but Mr. H. Graves Morris, of Luton, to whom the patient presented himself and who sent the teeth to me, has furnished me with an account of his condition before the teeth were extracted.

The patient was a man, aged 24, of massive build and well-proportioned frame. He had been the subject of severe neuralgia for some years and previously to consulting Mr. Morris had had all his lower premolars and molars extracted. These the patient described as difficult extractions, and his mandible had incidentally been fractured in the process. Therefore the natural inference is that his lower teeth were in the same condition in which his upper ones proved to be.

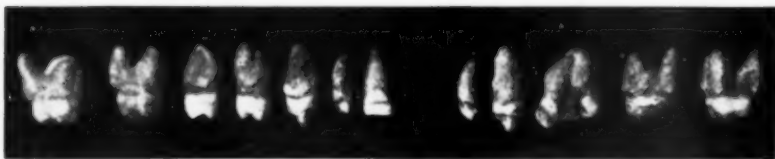
When he consulted Mr. Morris the whole of the gums of the upper jaw were very spongy, suggestive of pyorrhœa, but there was *no pus*. This condition refused to improve under treatment, and the neuralgia persisting, it was decided to extract all the upper teeth.

It will be seen that most of the teeth are very extensively exostosed, the incisors being least so. The two third molars and the left central incisor are missing, having been extracted previously, but it would seem

quite safe to presume that they were in the same condition as the rest. The two left premolars will be seen to be geminated by the overgrowth of cementum.

The first impression on examining the teeth was that it might be the result of a local infection from the gingival margin, but on closer examination one found no serumal calculus at all on the necks of some of the teeth and very little on the rest. Now if the condition were due to local infection from the cervical region, one would certainly expect to find a considerable quantity of serumal calculus from the pus which most assuredly would have been there, considering the length of time the condition had persisted. And, moreover, exostosis is not found associated with pyorrhœa in the ordinary way.

Therefore one must come to the conclusion that the cause was a general one, such as any of the general diatheses—for example, gout,



General exostosis of the maxillary teeth.

syphilis, &c.—or the administration of mercury. But, unfortunately, it is impossible to produce any history of this kind.

If anyone has any suggestions to make concerning the ætiology of the condition, or can describe any similar case that may throw some light upon this one, I shall be very pleased to hear them.

DISCUSSION.

Mr. LEONARD MATHESON asked whether the removal of the teeth resulted in the disappearance of the neuralgia or whether the mandibular teeth had also to be removed.

Mr. STANLEY MUMMERY said he had a similar case three or four years ago, although he did not think the exostoses were as marked, but the symptoms were very much more severe. The patient was a girl, aged about 23, and had continual neuralgia of a very bad type in paroxysms like tic douloureux, accompanied by violent sickness and prostration. The apparently sound teeth were removed until she became edentulous, and then her symptoms disappeared.

Mr. W. W. JAMES asked if the bones showed any change or there were any nodules on the alveolar plate. It seemed to him that there was clear indication of local irritation of the periodontal membrane which had produced a large amount of cementum and that a considerable amount of absorption had gone on round the apices of the teeth. The teeth were not equally affected as one would expect if the cause were a general one. He thought it was a local infection.

Mr. P. J. PROUD said that at a previous meeting of the Section he had exhibited models of a maxilla and mandible showing the bone very much affected. He extracted one root which was very much exostosed, and probably all the other teeth were in the same condition. There were distinct nodules, almost like bunches of grapes, round the necks of the teeth, and there was no pus. The patient was an old man, aged nearly 80, and a gouty subject. He said the condition had come on very slowly.

Mr. LEWIN PAYNE disagreed with Mr. James in his suggestion that a local cause was responsible for the condition. He considered that the history of this case and the state of the teeth pointed fairly definitely to a general constitutional cause as the primary origin of the trouble. Local irritation, if it existed, would be only, he thought, a contributory influence. The fact that the teeth were differently affected in the incisor and molar regions was in accordance with what usually occurred in exostosis. The frequency of exostosis had been estimated at 75 per cent. in the molar and premolar teeth, and 25 per cent. in those in the front of the mouth, so that although the incisors, in this case, were not so much involved as the rest of the teeth it did not eliminate the probability that the condition was due to a general constitutional cause.

Mr. DOWSETT, in reply, said all the lower teeth had been previously removed without curing the neuralgia. When all the upper teeth were removed the neuralgia disappeared. A denture was fitted and the man was perfectly comfortable. There was no change in the bones as far as could be seen; the gums were so spongy and thick that no bone could be felt enlarged, and unfortunately a skiagram was not taken. It was extremely difficult to say whether it was a local or constitutional affection, but the cause seemed much more likely to be a general one. Had it been due to a local infection one or two teeth would have been expected to be more markedly affected than the rest, but they seemed to be about all equally affected in the molar and premolar region. He was, however, open to conviction, as it was well known that there might be local septic irritation without any pus, giving rise to overgrowth of tissue.

Models showing Variation in Number, Size, and Position of Teeth, Incisors and Canines.

By T. CAMPBELL DYKES, L.D.S.

MR. DYKES exhibited a series of models which he had collected in the last few years, showing deformities of the teeth. One showed huge laterals which in the mouth measured $\frac{5}{16}$ in. across, and central incisors measuring $\frac{7}{16}$ in. Another showed central incisors of extraordinary size. A third model showed central incisors of different sizes, the right central incisor being narrower than the left central incisor. Another model showed six incisors in the upper and five in the lower, another conical-shaped lower incisors and canines. And another showed the left upper canine with a bicuspid mesial to it, the laterals being absent.

MR. SIDNEY SPOKES exhibited a model showing six incisors. It was a common thing, he thought, to get a supplementary incisor on one side but comparatively rare to come across cases with one on each side. He also exhibited a case of a canine tooth erupting in the middle of the palate in a boy, aged 9. The point of interest was a cleft in the mid-line of the palate, not running forwards nor backwards into the soft palate, the cleft having a specific cause, an unusual condition in a boy of that age. The boy evidently developed congenital syphilis as late as 8 years old. The canine tooth erupted a little while afterwards, so that the specimen showed the points of interest.

The Position of Swivels on Spring Dentures.

By DOUGLAS P. GABELL, M.R.C.S., L.D.S.

IF, in addressing you as to where to place the swivels for springs on a denture, I appear to resemble the person who tried to tell his grandmother how to suck eggs, my reasons are that our grandfathers did not treat the placing of swivels as a mathematical matter, did not know the movements of the jaw, and have left no reasoned account of why they

chose certain places, neither do they agree as to which place. One of the best authorities in this matter has felt it necessary to invent a sliding attachment for swivels, so that they can be adjusted after inserting the denture; and, furthermore, I find myself at variance with the very common practice of inserting a stop on the lower plate to prevent sagging of the springs. I shall not touch upon the advantages and disadvantages of springs, their strength, nor the technical details of attaching them, but shall rather attempt to apply our modern knowledge of the movements of the jaw to ascertain the best position for

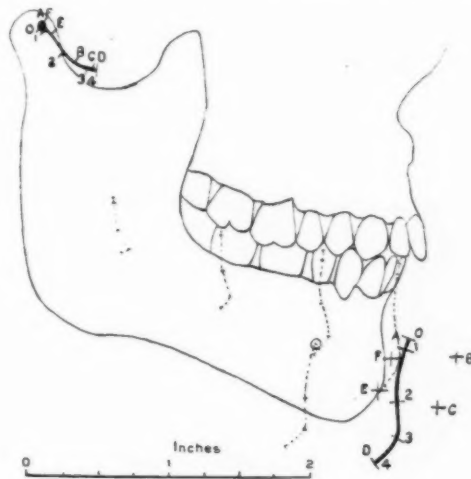


FIG. 1.

the swivels and the correct shape of the surface or chamber over which the springs work.

The factors concerned in the case are: First, that the action of the spring is an attempt to straighten itself, and the force exerted acts in a straight line from the two points of contact with the dentures nearest to the bend of the spring. Secondly, the shape of the surface on which the denture rests, the force of the spring being resolved into a pressure on to the surface and a horizontal thrust along the surface. Therefore, in each case one has to consider the direction of the force; firstly, with the mouth closed; secondly, when the mouth is open; and in each case to note what tendency to slip along the surface will be produced, and how the downward pressure will be distributed over the

gum surfaces. Another practical point to be considered is the position of the bend of the spring, as this often gives rise to pain by pressing on the gums or cheek, and is then not only painful but also introduces a new thrust.

As the basis for my argument on the action of springs when the mouth is open, I have taken Mr. Luce's and Mr. Norman Bennett's investigations on the movement of the lower jaw, which I believe to be thoroughly sound. You will notice that the movement of all the teeth is almost vertically downwards, although the anterior teeth travel a greater distance than the posterior ones.

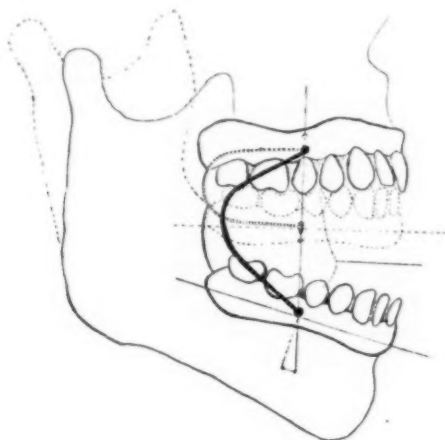


FIG. 2.

In the first diagram which I show you, I have carefully marked out this movement, and have added the outline of a jaw and teeth to make my meaning clear. To exemplify a variety of cases, I have applied jaws with very different shaped alveolar ridges to this same diagram, which, I think, is a justifiable procedure for our present purpose. I do not believe in any one conventional place for swivels, but in every case there is a best and many inferior positions. This best position will depend upon which part of the plate requires to be held up or down; how much room is available at the back of the mouth for the curve of the spring; what is the shape, position and resistance of the supporting surface under the denture. It is also desirable to keep springs and swivels out of sight and behind the curve at the angle of the mouth.

The vertical distance between the two swivels should be such that the spring does not straighten itself when the mouth is wide open, and is as little curved as possible with the mouth shut, both of which considerations depend on the length of the spring. Also enough room should be left for a protecting rim between the swivel and the edge of the denture without encroaching on the reflection of the mucous membrane over the buccinator, but the swivels should be as far from the line of bite as possible. The swivel head must not project so as to catch the cheek, but must be prominent enough to allow the spring to work just free of the teeth. A chamber or flat surface with a flat rim to hold the cheek away from the spring should be provided. The two

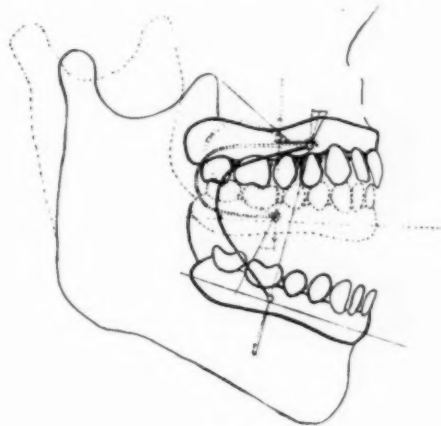


FIG. 3.

surfaces should be flat, parallel, or quite symmetrically converging and as near together as possible at the back to prevent abrasion of the cheek. The rim should be just clear of the spring when the mouth is closed and rise abruptly from the surface. But in special cases, to be described later, the rim is allowed to press on the spring and act as a "stop" or "block." Where no room can be afforded for this rim the spring can be "stopped" by several smaller devices. In symmetrical jaws the swivels, springs and chambers must be symmetrical.

I think that the rest of my communications could be better followed if I placed some diagrams on the screen.

Fig 2: I have shown the swivels placed immediately over each other and practically in the centres of the dentures, and when the mouth is

closed I think you will see that the action is to press the top plate up, the bottom plate down without any horizontal thrust, as the supporting base is in this case a horizontal surface; also the weight is evenly distributed over the whole of each base. But when the mouth is open quite a different condition exists, the lower swivel is still almost below the other, yet the supporting surface in the lower denture is now no longer horizontal, and the force resolves itself in a downward and a considerable forward thrust. The upper denture is not affected.

Fig. 3 appears to me to represent the best way to overcome this difficulty. The upper swivel is placed well forwards and the lower a little back. To make the pressure vertical when the mouth is closed,

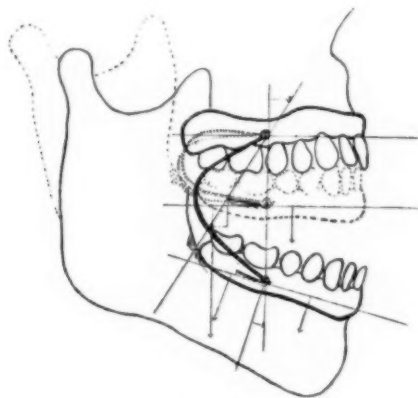


FIG. 4.

a stop has been inserted in the upper plate, the thrust with the mouth closed is thus kept vertical, but it must be admitted that the pressure at the back of the mouth is much greater than in the front. In the upper jaw with its very broad base and light pressure this is not likely to produce any ill-effect, but in the lower jaw with its narrow base posteriorly this certainly may result in an undue sinking. With the mouth wide open it will be noticed that the pressure is almost vertical on the lower denture and central; a little forward thrust remains owing to the impossibility of placing the swivel farther forward in the upper jaw for reasons already given, or in the lower farther back on account of the uneven pressure. In the upper denture there is a forward thrust, but from the shape of the mouth and the broad surface of

contact this will be found of far less importance than a forward thrust on a lower plate.

Fig. 4 shows what I believe to be a very commonly taught error in the adjustments of springs. In this diagram I have endeavoured to show a case where a usual placing of the swivels has caused the bend of the spring to impinge on the lower gum at the back of the mouth. The usual remedy for this is to insert a stop in the lower denture to prop up this spring; the result will be as follows: when the mouth is closed the thrust of the spring is strongly backwards in the lower jaw. With the mouth open it is strongly forwards, causing the lower plate

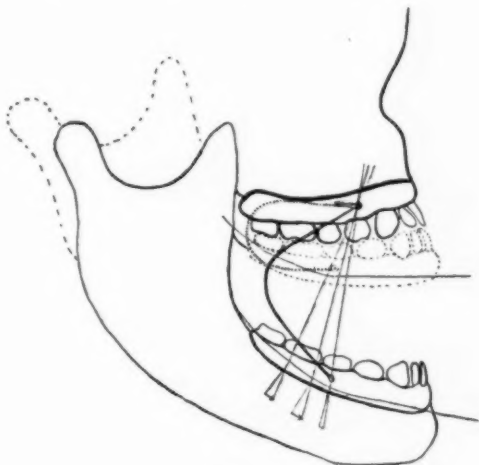


FIG. 5.

to shift considerably. Also the weight of the spring when the mouth is closed is thrown very heavily on the heel of the lower plate, a lesser trouble certainly than the impact of the spring on the gum, but bad enough. A better remedy than this lower stop would be, I think, to shorten the spring altogether, or, as I suggested in my last diagram, place the upper swivel forwards, which will raise the bend of the spring off the lower gum and also improve the direction of the thrust.

Fig. 5 shows another common trouble that has to be dealt with. A very close bite, a lower alveolus almost flat in front but curving markedly upwards at the back—the famous “slipping lower.” Here it might at first be thought that the upper swivel should be placed far

forward and the lower far back. But from the diagram I think you will see that if the lower swivel is placed over the curving surface the thrust of the spring will be forwards, whilst if it can be placed over the flat part of the jaw, this tendency is greatly reduced. Hence both swivels must be placed forwards. This is also necessary on account of the scanty room for the bend of the spring; a short upper stop will help to equalize the thrust. Keeping the weight forward in these cases is also beneficial.

On looking back into the literature of this subject I find that my predecessor, Mr. David Hepburn, advocates this forward position of the

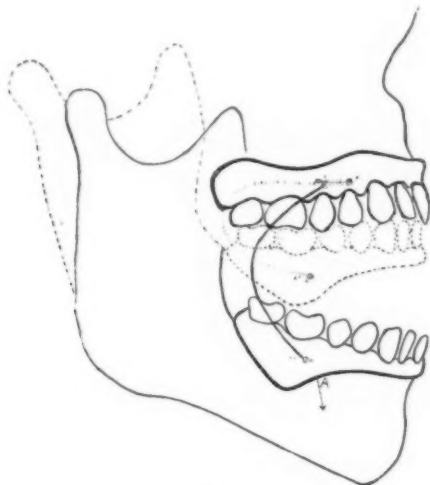


FIG. 6.

swivels in such cases, as the result of practical experience, but would also insert stops on both dentures to keep the bend of the spring off the gum.

Fig. 6 indicates another not very uncommon shape of the jaw, and is of interest as showing the importance of the shape of the base, and of equalizing the pressure. It is a case of very great wasting in the molar regions, with a moderate alveolus remaining in the incisor region. From the shape of the lower jaw it will be seen that no slipping is liable to happen. From the diagram you will see that if the lower swivel is placed over the bottom of the curve the pressure will be almost equally distributed on the gum at the back of the mouth with little

pressure in the incisor region; whereas if the swivel is placed rather farther forwards a very heavy pressure falls on to the part marked *A*, especially when the mouth is open. There is also a forward thrust further increasing this pressure, and the result is that the plate appears to require to be eased at this point, but such easing will not be found to give relief, as the spring pressure still urges the plate on the spot. Incidentally I may mention that should this condition occur where the natural incisors are standing, and a bar lower plate is worn, the trouble will be immensely exaggerated. This was pointed out years ago by Mr. Balkwill, but he does not suggest the movement of the swivel as a remedy, but the retention of a root underneath the plate. The points I have tried to bring out are that in determining the position of swivels a little diagram should be made showing the position of the jaws open and closed, and the shape of the supporting base and the best position of the swivels can then be calculated in a mathematical manner, from the consideration I have indicated in my communication, so as to ensure the least horizontal thrust, or the least harmful thrust when some must be left. The position of the bend of the spring can be determined also diagrammatically as I have done in my figures, but is much more easily found by trial on the wax dentures before trying them in the mouth.

DISCUSSION.

Mr. E. LLOYD-WILLIAMS sent the following communication: Mr. Gabell has introduced a subject of great mechanical interest, quite apart from any individual predilection as to the utility or otherwise of springs for the retention of dentures, especially in the light of what we may term our comparatively recent knowledge of the anatomical movements of the mandible. I may, however, state at once that from the general trend of the paper, if I have not misconstrued it, the complicated movements of the condyle—especially in their exaggerated form—may tempt us to make a false application of the underlying principles to the very practical matter of the adjustment of springs. What I mean is, that the mouth is only wide open or tightly closed for a mere fraction of the time that the dentures are being worn, and that for the rest of the period the lower teeth are separated from the upper by a *very slight interval*, and that in ordinary speaking and eating the interval is much less than we are accustomed to estimate. The due appreciation of this fact has an important bearing upon the mechanism we are considering. Mr. Gabell mentions two prime factors. The first is all-important; and if I might venture to restate it in its more important aspect—as it appears to me—I would say that “the

action of a spring is an attempt to straighten itself; and if one arm is longer than the other there is a *thrust forward* of that arm, while the action of the shorter arm is a *thrust backwards*." Possibly this simple definition may include at least a portion—and a very practical one—of the second factor. There is a third factor which the reader of the paper has omitted to mention, and that is that if the swivels to which the spring is attached are not parallel in all directions—that is to say, if the spring is not working on a true plane—the action becomes profoundly modified, and has a very disturbing mechanical influence, which would take too long to describe now. Another disturbing influence, which cannot be ignored, is found in the edentulous old—a class of patient who has most call for the support of springs: I mean the progressive changes and wasting of the mandible itself with a modification of the angle of the bone. This is a very important point to be remembered. Mr. Gabell has intentionally avoided the discussion of the "technical details" of attaching springs, but I have already mentioned one point, and there are two others, which cannot be divorced from the reader's treatment of the subject. One is the *strength* of the spring, which, if it is too strong, will be a most important factor in producing some of the disasters described. It will seldom be necessary to use anything stronger than what is known as No. 7. The other point which refuses to be ignored, the subject-matter of the paper, is the relation of the distance between the swivel heads and the length of the spring used. There can, of course, be no hard and fast rule about this, but as a matter of experience it is found that if a spring is $1\frac{1}{4}$ in. long it is advisable to separate the swivel heads by a distance of $\frac{3}{4}$ in. Any great variation from this proportion will militate against success; and, in spite of every precaution which may be taken in this as well as other respects, the complicated lateral masticatory movements of the mandible—especially in the very old—may upset all our calculations. The latter trouble may, however, be considerably lessened if Rogers's swivels are used, the revolving barrel on the shank of the swivel allowing for a good deal of auto-adjustment. As a rule I discard anything in the shape of a "stop" for the upper, but a properly constructed "rest" or shelf is always advisable for the lower and it should be continued as a shoulder in front of the swivel head, thus serving as a shield for the buccal tissues. I have prepared a little bit of apparatus which will serve to illustrate very simply some of the points I have touched upon, especially that of the relative positions of the swivel heads—and therefore of the springs—in various movements of the mandible. I have only had a few days, since reading the paper, to prepare this little experiment; but had time permitted I should have made something more elaborate, with adjustable swivels and sections of teeth articulating as they would in the mouth. I should also have liked to show the movements in the mouth of an elderly person, instead of those of a young adult, aged 31, who is the subject of the experiment I have the pleasure of showing the members to-night. I should like to be permitted to thank Mr. Gabell for his interesting notes on an interesting subject.

The PRESIDENT (Mr. H. Lloyd Williams) said the members had all enjoyed the paper, although many had very little experience of the use of springs. He himself had used springs on such few occasions that he had no experience worth mentioning. The improvement in the knowledge of the movement of the mandible was very marked. Mr. Norman Bennett's paper showed graphically the movements of the mandible and thus laid down a scientific basis for such work as this of Mr. Gabell, whom he heartily congratulated upon making such excellent use of that paper in treating the subject, thus reducing the adjustment of springs to a matter of scientific accuracy and certainty.

Mr. STANLEY MUMMERY said Mr. Gabell had observed that the movement of the teeth was vertical in the incisor, bicuspid and molar regions and that when the mouth was opened the incisors moved through a larger distance than the molars, and he could not see how the two statements were compatible. In inserting a prop into the mouth of a patient one realized that the incisors were separated by a considerably greater amount than the molars. If the movement was truly vertical in the incisor and molar region the separation should be the same when the mouth was open. It appeared to him that the fact that the separation was greater in the incisor region than in the molar region indicated that the movement was in the nature of a hinge.

Mr. LEWIN PAYNE considered the knowledge of springs was exceedingly limited at the present time, and therefore the thanks of the Section were due to Mr. Gabell for calling attention to what was an important subject, although now only limited to exceptional cases. The fact that most of the text-books said little or nothing concerning the points Mr. Gabell had raised more than justified the paper. It seemed to him the use of spiral springs applied specially to mouths in which there was deformity in some form or other, to cases in which dentures had to be applied after the removal of a malignant growth, and also where an obturator had to be inserted in connexion with cleft palate. With regard to accuracy in the application of springs, there were peculiar difficulties in some cases, especially in those where the greater portion of a mandible had been removed. Personally he had found it necessary in some cases to reverse the bow of the spring on one side of the mouth to compensate for the pressure on the other. He would like to ask if Mr. Gabell could give any further information concerning such abnormal cases and whether he had also experimented in cases where the muscular pressure was not equal on both sides of the mouth.

Mr. W. W. GABELL said he had used springs not only in abnormal cases but in ordinary cases, as there were some patients who could be made more comfortable by the use of springs than without. The effect of the interposition of a peg, or touching against a shoulder, was certainly a new point, and had brought to his mind the reasons for some failures. He suggested that the ignorance of the mechanism of a spring was some reason for their falling into disuse. If the points mentioned in the paper were carefully considered they might be found very useful in practice.

Mr. CARL SCHELLING said that in a spring which had a stop to the swivel, the bend coming upon the spring where it was fastened to the stiff end of the shank would cause the spring to wear out much sooner than a spring fixed to a swivel that was free to play.

Mr. SPOKES said he had had the usual limited experience in the use of springs in ordinary cases, the greatest assistance he had derived from the use of a spring being in cases where a large portion of the maxilla had been removed and perhaps the floor of the orbit was missing, and something had to be done to make the patient more or less comfortable and keep food within proper limits. On several occasions he had found it satisfactory to have a little light frame on the teeth in the lower jaw simply to carry the swivel to support the obturator on the same side. There were certain cases in which the obturator could not possibly be kept in at all without some such device. He thought Mr. Gabell's suggestion as to studying the facts of each case was of great importance, because it depended entirely on the surrounding tissues and on where the pressure was going to be, as to where the two points of the spring should be arranged.

Mr. E. BARTLETT said he had had a great experience extending over years of springs and swivels, although he used them very seldom. Each case required different treatment, and it was difficult to lay down any hard and fast line. Generally in an ordinary case he had taken a fixed point in the lower, for instance, between the first molar and second bicuspid, and made his upper accordingly. Unless it was absolutely impossible, he had a good groove counter-sunk in the lower, so that the spring should not rub against the cheek. He made it a rule in the upper to try one spot, the middle of the second bicuspid, and see how it worked out with the lower point fixed. Nine times out of ten he had found that was far the best place to get vertical movement and no thrusting forward of the lower or interference with the upper. He did not use any fixed stop on the upper to prevent the swivel going up, as he did not find it necessary, because if it did bulge up a little, provided it did not touch the jaw and cause soreness, it helped to keep the lower down and backwards, overcoming the pressure of the tongue to put it forward. It did not do to trust to the lip, because the lips, in old people especially, were often very thin. He had not worked out the matter scientifically, as he had always tested each individual case, keeping a series of small swivels with various sized plates that he could put in and try how they worked. He seldom used springs now except when plates became very loose, and then he put springs and swivels on for a few months until the jaws had settled and he could make new pieces.

Mr. DOUGLAS GABELL, in reply, said he advocated, on mathematical lines, that the upper swivel should almost always be put farther forward than usually advised, and directly that was done an upper stop became necessary. The members who had spoken appeared to have been surprised at the upper stop, but that was because they put the upper swivel far back. It was also necessary

to consider the shape of the foundation on which the plate rested when determining where to put the swivel. The old-fashioned way was to fix the swivel somewhere and try it, and when a spot was found which the patient would put up with that was considered the right position, although it might only be a spot which would just do. With regard to the lower dentures slipping forward, it was quite probable they did, the reason being that the upper swivel had not been placed far enough forward. If Mr. Bartlett had started by placing his upper swivel over the first bicuspid, it was probable he would have come to a happy resting-place very much sooner, provided that he also used the upper stop so as to prevent the wrong action when the mouth was closed. With regard to the groove for supporting the spring in the lower, if the upper swivel was put back a groove was necessary in the lower in order to prevent the spring from pressing down on to the lower gum, but it was not by any means a necessity, because if the upper swivel was placed forward it would leave the spring quite free from the lower gum. With regard to springs being not much used in practice, when Mr. Coxon read a paper in 1896 he stated that in that year the firm of Ash and Sons sold 10,000 pairs of gold springs per annum. Before bringing the subject forward that evening, he himself had inquired what was the present state of affairs, and was informed that the sales continued to 1901, and since then the sales had decreased by one half. There were many more firms than there were formerly, and yet one firm still sold 5,000 pairs of gold springs per annum! They were all supposed to be used in connexion with cases where the lower jaw or the upper jaw had been removed! He had tried to bring out that the placing of a swivel was not a mere matter of trial but that the right way was to find what was the direction of the action of the spring, and what was the surface which had to support that spring, and then to calculate with certainty what the position of the spring ought to be. That he had attempted to do for the ordinary cases met in practice, and there was no reason why the same thing should not be done in connexion with cases of deformities. He was told that old people—who also, it was allowed occasionally, wore springs—had very erratic movements of their lower jaws, but he did not think that would make any difference, because though the condyle path usually became flatter, they could only move their jaws in the way the condyle would permit, and the permission of the condyle was for the lower jaw to come forward. The condyle did not permit much backward movement. If the upper swivel was placed further forward than had been the practice he thought it would be found all the troubles would be overcome. With regard to the question of when springs should be used, he had purposely avoided that point, as it did not seem to affect the subject. The strength of the spring had been mentioned as making a difference in its action, but that was not really so. The strength, of course, exercised more pressure on the gums, and it was wise to use the weakest spring possible, because lower gums, when they were narrow, would not stand very great weight. The distance from swivel to swivel was a question he had not dealt with as affecting the action of the spring. It was said in the books that if swivels were placed so close together that instead of

the end of the spring being straight it curved in at the front end, the action would be to throw both plates forward. How a spring could act forward on both swivels was a thing he could not understand. Testing the case with the little apparatus he had brought with him, it would be found that whether the swivels were placed wide apart or close together, the action of the spring was still straight from swivel to swivel. The Rogers swivel was certainly a very useful little apparatus, and would save the wear and tear on the spring very much. With regard to the stop wearing out the spring, if the spring rubbed up against the tooth—i.e., if there was a lateral push on the spring—it would be worn very much indeed, but a stop to prevent the spring tending upwards or downwards would not be found to wear the spring because the spring came flat upon it, and there was no rubbing unless there was considerable lateral movement in the jaw. If that was of any importance, the introduction of Mr. Coxon's swivel with a stop inside the swivel itself would effectually prevent it. The only objection he had to Mr. Coxon's swivel was that it was rather too neat, and if it was not put in perfectly accurately in the first place there was no means of adjusting it afterwards without taking the swivels out; whereas an ordinary shoulder of vulcanite or a little gold ledge could be adapted after the plate was made without re-making the plate. He agreed with Mr. Spokes that each case should be studied in itself, but it should not be by trial and error but by a study of correct principles. With regard to Mr. Mummery's remarks on the movement of the jaw, that if all the teeth moved down vertically one could not go further than the other, that was absolutely correct, and he had protected himself in the paper by saying "practically vertical." The diagram showed it was almost exactly vertical in the place where the swivels were. The little apparatus Mr. E. Lloyd-Williams had prepared was very interesting indeed. He had seen it for a few minutes before the meeting and had tried to take a tracing of the movement of the swivel on a piece of smoked glass, but he could not get a very accurate tracing, although as far as he could make out the action bore out the diagram. Mr. Lloyd-Williams spoke of the resting position of the jaw, and Mr. Norman Bennett had worked out that position with the teeth slightly apart, and the points on diagram 1 showed the resting positions of that particular jaw. The parts marked O represented the jaw tightly shut. The movements from the tightly shut to the resting position were practically vertical. Also the movement lower down from the resting position was practically a vertical movement. He was very glad that nobody had proved him wrong in any of his facts, but sorry to hear members still say that the lower shoulder was right and that the swivel must be placed over the second bicuspid—that as things had been done so they ought still to be done.

Subsequently Mr. Gabell understood Mr. Schelling to mean that a stop in the swivel head or on its shank would cause the spring to wear out at the end of the shank. This was quite true.

Odontological Section.

April 22, 1912.

Mr. H. LLOYD WILLIAMS, President of the Section, in the Chair.

"Dermoid Teeth," or Teeth developed in Teratomata.

By W. McADAM ECCLES, M.S., and A. HOPEWELL-SMITH,
M.R.C.S., L.D.S.

"DERMOID TEETH," or teeth developed in teratomata, are of interest to the embryologist, the pathologist, the surgeon, and, we believe, to the dentist. Teeth appearing elsewhere than in the maxilla or the mandible must be considered as abnormal. The origin of such teeth is now believed to be almost certainly connected in every case with a teratoma. These teratomata occur most commonly in the ovary, in the neck, and possibly in the testis. They are seen in the human subject, and also in animals of a lower grade. When occurring in the neck, a teratoma is probably an anterior dichotomy, abortive in most cases. It is not our intention to refer to the teeth or denticles which are seen in this form of tumour. We shall confine our remarks to the dental structures which are by no means infrequently discovered in those cysts which are not uncommonly associated with the human ovary, and which have been for long termed "dermoid cysts."

After the brilliant paper by Mr. S. G. Shattock [3] there might seem to be but little ground left for any further reference to these cysts and the teeth developed in their vicinity, but as the subject has not yet, we believe, been brought before a meeting of the Odontological Section of the Royal Society of Medicine, we have determined to do so. There were, however, three earlier British papers on the subject. In 1860, Mr. Salter [2] published an excellent account of these teeth, while in 1863 Mr. Alfred Coleman [1] presented another, and in 1890 Mr. T. Charters White and Mr. J. Bland-Sutton [5] jointly read a most instructive contribution to the subject. Twenty-two years have passed

since then and it may not be amiss to once more review our knowledge of these significant structures.

When examined, an ovarian "dermoid" is found to be a true teratoma.

"DERMAL" TISSUES.

For our purpose in this paper, it is interesting to note that it is what may be called the "dermal" tissues which seem to be most in evidence. There is abundance of skin, often much hair, and this of two kinds, fine lanugo-like, and long and scalp-like, each growing from its own appropriate part of the foetus, and teeth, sometimes only one, often many, and occasionally exceedingly numerous. Also in a few instances nails or horny structures have been observed.

RELATION OF TEETH TO TERATOMATA.

The exact position of these teeth in relation to the teratomatous tissue and to the actual cyst wall is a matter of some interest and importance. The teeth may be found (1) embedded in bone in actual alveoli or sockets, (2) embedded in soft tissue, either of the foetus or possibly of the cyst wall, or (3) free within the cyst cavity.

There is no reason why a teratomatous foetus should not possess an ill-formed maxilla or mandible, and no reason why such a jaw should not carry teeth. Hence the appearance on, or in the tissue forming the foetus, of bone with attached teeth is easy of explanation, but it is difficult to account for those instances where teeth have been found at some distance apparently from the actual site of the foetal tissues, and attached to soft tissues only. There are three possible explanations: First, that during the development of the cyst, associated with which is the foetus, pressure has caused a lateral displacement of a part of the foetus, so that the tooth-bearing area has, as it were, become flattened out, leading to an elongation of the tooth-band. Secondly, there may have been a homologous twin which has developed very much less than its fellow, in fact, the teeth may be the sole evidence of its existence. It is possible for the same ovary to contain three separate teratomata, or triplets, as is shown in a specimen in the Royal College of Surgeons Museum,¹ and thus for the number of teeth present to be considerable, and their position remote in relation to the obvious teratoma. Or, thirdly, it may be an anterior dichotomy of the teratoma, thus allowing for at least a second set of teeth.

It is interesting that it is always the cephalic end of the teratoma in which these "dermoid" teeth arise, and, in fact, the dental structures may in some instances be the only evidence of the cephalic end of a trunkless (acormous) teratoma.

VARIETIES OF TEETH.

The morphological variations in teeth associated with ovarian teratomata approximate very closely to those usually found in the human mouth. Incisors, canines, premolars and molars have their counterparts in these cysts (figs. 1 and 2). The premolariform and



FIG. 1.

The bony contents of a teratomatous ovarian cyst, being a collection of extremely irregular plates and spicules of bone containing teeth lodged in deep alveoli and mostly resembling bicuspid.

From a woman, aged 27. The tumour was of such extreme hardness as to resemble a fibrocystic uterine growth. Its surface was uneven, its interior multilocular, consisting of chambers lined with skin and adipose tissue. The skin contained numerous sebaceous glands, and from it grew light-coloured straight hairs. The chambers were distended with a yellowish-white, grumous, fatty emulsion, with loose hair matted into balls. The bony growths were embedded in the stroma, and projected into the chambers of the cysts. (Royal College of Surgeons of England Museum, Gynæcological Series, No. 70.)

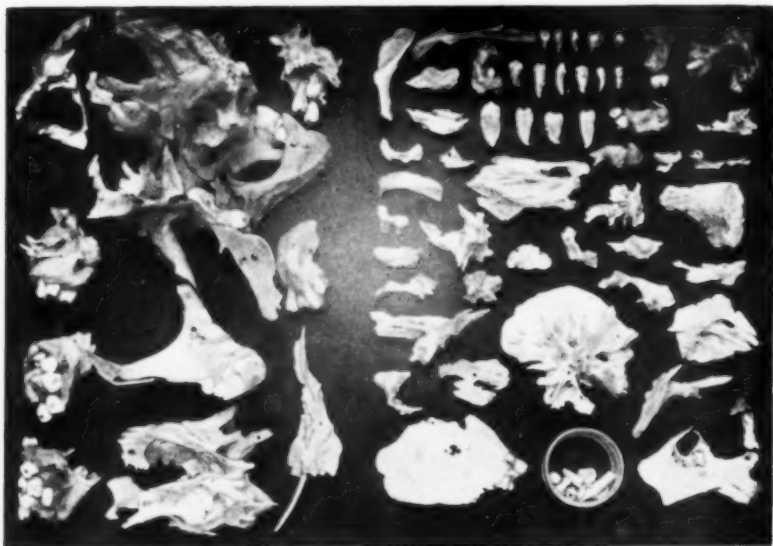


FIG. 2.

Bones and teeth from a teratomatous ovarian cyst. On the left are nine bones of considerable size, several bearing teeth. The largest, nearly 6 in. in long diameter, is of extremely irregular form and made up of straggling processes of thin bone curving in all directions. The uppermost is spongy; the lowest, much firmer, shows two teeth imperfectly cut; and one in the middle bears two conspicuous molars. On the right nearly forty smaller bones are arranged, some dentigerous. They vary greatly in form: one resembles part of a parietal bone in a fœtus, another the squamous portion of the temporal, but none bear any likeness to bones of the trunk and extremities. There are also fifteen well-formed teeth of all types not attached to bone, and some more in the glass box in the lower part of the specimen.

From a girl, aged 18. She had not begun to menstruate till six months before the removal of the tumour, which she had noticed for four years. The external surface of the tumour was extremely irregular, some of the protuberances communicating with the large cyst by short hollow pedicles. The interior was one large cyst with thick walls, containing many other cysts within growing from the inner surface. Many parts of the walls of these cysts were cartilaginous, with centres of ossification; the lining membrane resembled skin, and the contents were an emulsion of fat and mucin, with scanty collection of hair-balls. These specimens lay in the stroma of the tumour. The uterus and opposite ovary were scarcely developed. (Royal College of Surgeons of England Museum, Gynæcological Series, No. 72.)

caniniform types predominate from the point of view of number. The teeth themselves are generally well developed, and bear few, if any, traces of any degeneration of their exposed portions. Seldom, if ever, have purely conical representatives been noticed in these cysts. Sometimes, however, very numerous malformed dental bodies are met with. These possess but little resemblance to ordinary human teeth.

The cause of such enormous quantities of these denticles is difficult to determine. It may be that an extended tooth-band has given rise to myriads of aborted, but more or less calcified, tooth-germs. Or that fenestration and total disappearance of the intervening portions of the tooth-band have occurred in the usual way, and that arrest of complete development, caused by the abnormal environment to which they have been subjected, coupled, perhaps, with the precocity and rapidity of their growth, has resulted in the display of congeries of misshaped, irregular masses composed mainly of enamel and dentine. Although these teratomatous cysts are tooth-bearing cysts, they are in no sense dentigerous cysts, and it would appear to us to be extremely likely that the same operations of pathogenesis may be acting here as in similar fashion to those which act sometimes in the jaws. It is not beyond the bounds of possibility that there may be occasionally a multiplicity of tooth-bearing cysts, which ultimately are capable of becoming incorporated in one large cavity.

ERUPTION OR NON-ERUPTION OF TEETH.

Of the actual dynamics of the eruption of ovarian teeth it is impossible to speak. Many of the oral conditions which assist this phenomenon are entirely absent. The growth of bone when present may have some bearing upon the eruption, but this cannot hold in those instances in which teeth are erupted from the wall of the "dermoid" in places where no bone exists.

Many cysts contain enamel organs which have not proceeded to maturity. It would seem that many teeth while fully developed, except perhaps as far as their roots are concerned, do not become extruded through the superficial soft parts, though evidences are not wanting that generally, by virtue of their rapid and precocious growth, they do completely erupt on the surface of the teratoma.

There is no evidence of any eruption of a second dentition such as occurs in the normal mouth.

SHEDDING OF TEETH.

In the ovarian embryomata hair is frequently shed. The same cause may be at work in producing this separation as in the case of other epidermal derivatives. The implantation of the ovarian teeth is comparatively feeble in character. They are retained in the fresh condition by a thin annular elevation of connective tissue at their necks, and in many dried specimens there is an appearance as if the marginal bone had become absorbed, or, at all events, had never been fully developed. The necks of the teeth are well exposed and vary in depth, and often their roots are visible above the free surface of the bone alveolus.



FIG. 3.

Enamel and Nasmyth's membrane. ($\times 95$)

It is possible that when a tooth is found free within the cavity of the cyst, it has been shed by senile changes, in an acardiac, acormous parasite as part of a pathological retrogression which is entirely different from, and antecedent to, that of the host. But in other cases it may but be an accidental detachment during the extraction of the cyst from the body.

THE ANATOMY OF THE TEETH.

For the most part the teeth found in ovarian teratoma exhibit the main characteristics of those of the human permanent dentition, though on the whole they are smaller. In those examined they measured about

5.5 mm. in their extero-internal diameter (which would correspond to the bucco-lingual direction in the mouth) and 17 mm. in extreme length. But, of course, many variations of mensuration are met with. In those specimens specially examined for the purpose the translucent pellicle of Nasmyth's membrane was present (fig. 3).

A root is generally present, being joined to the crown sometimes without the usual cervical constriction. Seldom is a tooth bi-rooted, a multi-rooted tooth being very rare. The roots taper to a point.

On section a pulp cavity with root canal can usually be observed. In extremely thin incisiform specimens this is often narrowed down to



FIG. 4.

Irregular distribution of the dentinal tubes. ($\times 95$.)

an inconspicuous canal, and even this at times may be wanting. In the fresh condition pulp tissue is present, and on the authority of Messrs. Bland-Sutton and Charters White nerve-bundles can be seen accompanying the blood-vessels. When no actual cavity exists, dentinal tubules radiate more or less from a common centre outwards, but one of us has found, in some sections, the tubules running centripetally as well as centrifugally (fig. 4).

Enamel, dentine and cementum are present. The first is fairly normal, the second of an incompletely developed character, as proved by the abundance of interglobular spaces. Cementum is frequently

absent. If it is present, it constitutes a very thin external band of the dentine, just beyond the homogeneous layer and the granular layer of Tomes (figs. 5 and 6).

PATHOLOGY.

The pathology of these teeth has been cursorily described by Wedl [4]. He believes that erosion of the superficial parts may take place. He has not seen dental caries, which is to be expected, inasmuch as the contents of the embryomatous cyst are generally of a thick alkaline nature, and suppuration often occurs. Mr. Shattock says that odontomata (enamel nodules) may sometimes be seen upon the roots. The teeth are clumped together, and are misplaced when found embedded in the teratomatous bone. Instead of occupying a definite relationship to each other, as in the mouth, they are placed irregularly with regard to one another, possibly from the fact that here there are no mechanical factors such as are produced by the action of the soft tissues of the tongue and cheek or lips in giving rise to the proper alignment of the teeth in the dental arcade.

BONE IN WHICH THE TEETH ARE FOUND.

Some of the pieces of bone in which these ovarian teeth have been found are exceedingly like small maxillæ or ill-developed mandibles. One peculiarity, however, is often present, namely, that whereas the size of the "jaw" itself is much less than the size of the jaw of the host, the teeth themselves found in the ovary may be almost, if not quite, as large as those found in the normal mandible of the host. The bone itself is of poor quality, and consists mainly of cancellous tissue (figs. 7, 8, and 9).

RELATION OF THE "DERMOID" TEETH TO HAIR.

As a rule the teeth in the teratomata of the ovary bear no relationship to the hair growing from the same parasite, other than that the teeth will be found in their own normal position in reference to the cephalic end of the teratoma, and the long hairs will be springing from the scalp portion of the foetus, also at the cephalic end. But in one specimen which we have observed, short, rather stubby hairs were found growing, in a ringlet, actually round the neck of the tooth from the soft tissue which might be said to be forming the gum. This fact is interesting as showing the close possible connexion between the two dermal structures, hairs and teeth.



FIG. 5.

Vertical section of the enamel. ($\times 55$.)



FIG. 6.

Imperfectly formed dentine. The upper margin is the homogeneous layer. ($\times 95$.)

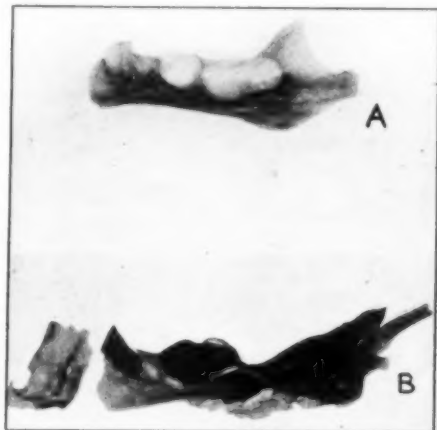


FIG. 7.

Skiagrams of (A) normal fetal mandible; (B) "mandible" bearing teeth from "dermoid."

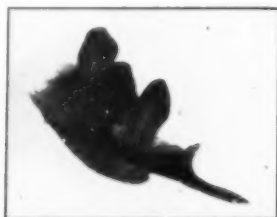


FIG. 8.

"Dermoid" teeth in "dermoid" bone.

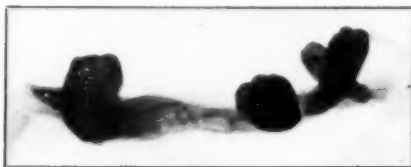


FIG. 9.

Skiagram of four "dermoid" teeth attached to a small piece of "dermoid" bone.

X-RAY EXAMINATION OF "DERMOID" TEETH.

The X-ray examination of "dermoid" teeth is interesting from several points of view. The teeth, as normal teeth, obstruct the passage of the rays more markedly than does the bone by which their roots may be surrounded. Hence it is quite possible that an X-ray examination of a living subject who is the host of a dermoid cyst of the ovary

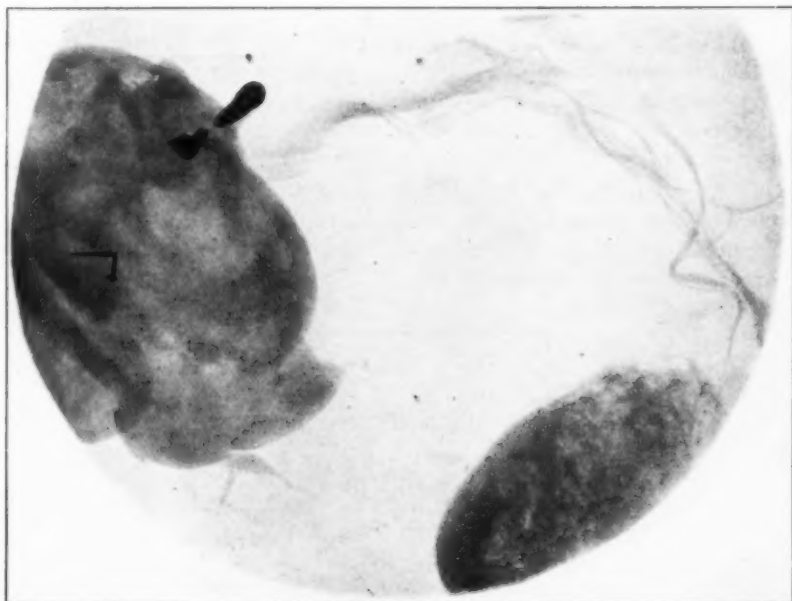


FIG. 10.

Skiagram of a dermoid cyst of the left ovary from an unmarried woman, aged 37, showing teeth and scalp hair growing from the cephalic end of the teratoma.

might reveal the presence of the cyst by the marked shadow thrown by the teeth, if any were present, in contrast to the shadow thrown by the pelvic bones.

A skiagram will also indicate the presence of a pulp cavity in the interior of the "dermoid" teeth. It will also show the character of the bone associated with the teeth, if any bone exists (figs. 10 and 11).

"DERMOID" TEETH IN THE TESTIS.

There are on record several cases of a dermoid cyst of the testis in the human subject, but the condition must be considered as an extremely rare one. A similar cystic enlargement of the testis of the horse is not so uncommon, and particularly where the testis is retained.

One case at least, occurring in the human subject, presented a tooth borne by the teratoma in the testis. In the case of a horse there have been found similar teeth.

While the origin of ovarian "dermoids" may now be considered as settled, it is difficult to conceive that the testis can be the host of a teratoma with an identical origin. Mr. Shattock has put forward the suggestion that these "dermoids" of the testis are in reality teratomata of the ovary portion of an ovi-testis gland in a true hermaphrodite. This is certainly quite feasible, and some amount of confirmation is obtained from the presence of a teratoma associated with an imperfectly descended testis in a "rig" horse. Such an animal is not infrequently vicious and unsuitable for domestic purposes. The removal of the retained testis has the effect in many instances of rendering the animal docile and useful.

CONCLUSIONS.

(1) The presence of teeth in dermoid cysts of the ovary, and of the testis, tends to prove the teratomatous nature of these tumours.

(2) The similarity between dermoid cyst teeth and those of the normal human mouth tends further to indicate their teratomatous origin.

(3) The period of eruption of the "dermoid" teeth does not coincide with the period of eruption of the teeth of the host, but is probably earlier, and their growth is more rapid. It is possible that this precocity may be due to the influence of the super-host through her blood.

(4) There is no distinct evidence of the shedding of "dermoid" teeth, and there is no evidence of any distinction between a deciduous and a permanent dentition.

(5) While "dermoid" teeth may be ill-shapen and may otherwise deviate from the form of normal teeth, there is no evidence of any pathological process which can be termed "caries."

(6) An examination by X-rays should be made of every case in which an ovarian "dermoid" is suspected. It is probable that "dermoid" teeth will throw a shadow, and this shadow will be a help in the diagnosis of the condition, and lead to the early and safe removal of the cyst.



FIG. 11.

Skiagram of a dermoid cyst of the left ovary from an unmarried woman, aged 32, showing forms of teeth, cancellous bone.

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DISCUSSION.

Mr. BLAND-SUTTON said he had listened to the paper with the keenest interest. The first time he ever saw a dermoid cyst was thirty-two years ago; it contained grease, teeth, and hair; it made a profound impression on his mind and his interest in dermoid cysts had continued to the present time. He read a paper before the Odontological Society dealing principally with the anatomy of the structures found in ovarian dermoids, but since that time a large amount of work had been done on the origin of these tumours which threw a great deal of light on the question. He was a little handicapped in discussing the subject, because he was dealing with this subject before another Society in a few weeks' time, and he was anxious not to forestall some of the things in that paper. The interesting question with regard to ovarian teeth, a question which had been asked by his friend Mr. Alban Doran over and over again, was how it was that dermoid cysts contained so many teeth. It had been realized more and more in recent years that ovarian dermoids were really products of the sex-cells. There was a very remarkable specimen in the Museum of the Middlesex Hospital, described by Mr. Moore in 1867; when it was removed it must have been nearly as large as a football, and it was thickly dotted with ovarian teeth. There was also one in the Museum of St. Thomas's Hospital weighing many pounds, and it contained hundreds of teeth. The presence of so many teeth could not be due to one sex-cell, but to many, and he believed that in all probability it was due to segmentation of mature ovarian ova. It was well known that ova underwent maturation in the ovary and then disappeared, and there was evidence, he believed, that they could be stimulated to go on to develop independently of that great and powerful stimulant, the spermatazoon. One of the most important facts that had been learnt in regard to the ovarian dermoids was this: for many years they had been regarded as some of the most benign tumours which attacked women, but, in recent years, it had been realized that there was a malignant form of ovarian dermoid, as malignant as any tumour known to attack women. They occurred in young girls and young women, grew with great rapidity, and spread like cancers, causing secondary deposits in the peritoneum and the liver and the lung. These secondary deposits, when they came to be examined, were found to contain not only hair and skin, sebaceous glands, neuro-epithelium and pigmented retina cells, but also enamel organs and dentine papillae; such things could only come from the segmentation of ova. But it was curious to find in tumours produced in that way there should be such a display of malignancy. Another question often asked was why they should occur in the testicles. They were, however, very rare in that position. Students were taught that one of the varieties of tumours of the testicles to put down in examination papers was the dermoid, but, as a matter of fact, a dermoid of the testis was an extremely rare thing. In the literature of this country only five cases had been described in the last twenty-five or thirty

years; two of those cases he himself had secured, and both came from abroad, one from China and one from India. In the horse, dermoids had often been found in undescended testes, and the teeth had the same character as the teeth of the horse. A distinguished veterinary surgeon, Mr. Hobday, had been very interested in the matter, and had given him opportunities of studying specimens. The dermoids did not occur in the secreting structure of the testes, but in the tissue known as the rete testis which contained ovarian vestiges. Some interesting work had been done on what was called "parasitic castration" in spider-crabs, which went to show that under certain conditions ovarian tissue occurring in the functional testes of the male produce ova as well as spermatozoa. During the last fifteen years some interesting facts had been brought to light in morphology which would go to prove the contention he had always maintained, that those tumours called testicular dermoids were not really dermoids of the testes but grew in the remnants of ovarian tissue in the rete testis. Some of the younger Fellows of the Society should carefully examine ovarian teeth and determine whether the pulp possessed nerve fibrils. He was also sure that the appearances in ovarian teeth which resembled the effects of caries were gaps in imperfectly developed teeth which contained soft tissue before they were macerated.

Professor KEITH said he had very little to add to what Mr. Bland-Sutton had said. He had paid some attention to the teeth of dermoids with the view of obtaining some suggestions as to the primitive type of teeth in the human race, to see if light could be thrown on the probable origin of man, or of his teeth, but, so far as he had gone, the result had been really negative. None of the teeth were really incisors, properly speaking. The premolar teeth were not like any premolar teeth he knew of or could conceive to be in the human race. The molar teeth also were unlike any molar teeth that had ever existed. He had come to the conclusion that it would be in vain to seek in dermoid cysts for any assistance in deriving the genealogy of the human race. He doubted whether very much light would be thrown on the human teeth by dermoid cysts. With regard to the much wider subject which Mr. Bland-Sutton had opened up, as to the origin of the teratomata, he was all at sea. He did not know why teratomata should occur more rarely in the testes than in the ovary, because it seemed to him that the primordial ova of the male testicle were not essentially very different from the primordial ova of the female, and he saw no reason why teratomata should not be quite as common in the male as in the female; but the fact was that they were not, and there must be an explanation. He thought that teratomata were proliferations of a certain kind of tissue, that any little bud which might be hidden away in the tissue derived from the epiblast when it started to grow would develop skin. The whole nature of teratomata was still most obscure, and at present the theories were in the nature of rather wild guesses.

Mr. ALBAN DORAN said the ova of a normal ovary could do a great deal. Under certain conditions they could make a man with all his tissues in order; in the "dermoids" the ova made something human, but with all the tissues in

disorder. He thought there was too much readiness to think teratomatous cysts were quite different from the common cystic adenoma of the ovary. There was little reason to believe that either arose in vestigial relics like the common papillomatous cysts of the ovary and broad ligament. Was the common cystic adenoma so very different from a teratomatous cyst? An ovary had the bad habit of producing very often a tumour composed solely of the most elaborate glandular tissue. A human being produced by ordinary impregnation included much glandular tissue, but in its right place. The adenomatous growth was due to some unnatural stimulus, and it would be rash to say, as general pathologists admitted, that an adenoma of the ovary was in every respect the same thing pathologically as an adenoma of the breast. Histologically, under the microscope it looked similar, but the conditions were very different. It might be said logically, that whereas the ovary had a bad habit of producing a tumour all glandular, it had also another bad habit of producing a tumour of all sorts of epidermic tissues, which sometimes massed together to form a teratomatous acormous foetus; but it was not like the acormous foetus which was parasitic on a normal foetus, the pair being uni-ovial twins. It was well known that a big mass of teeth was never found in the acormus, nor great scattered tufts of hair. On the other hand, it was only experts like Mr. Bland-Sutton and Mr. Shattock who were able to find, occasionally, a complicated nervous system and a trace of bowel in an ovarian teratoma. The inexperienced might find no teeth in a teratoma, but an expert like Mr. Bland-Sutton might detect them embedded in masses of softer tissue. What was the meaning of the presence of teeth? They were sometimes found with bone, and sometimes with no alveolus of any kind. He thought Shattock's theory was the most correct, that dentigerous epithelium, or gum tissue, developed originally in a small area on the inner wall of the cyst. Growth of the cyst wall occurred just as in the common glandular cysts. In the common cyst the glandular tissue grew with the cyst wall, and when there was much stretching, plugging of vessels, &c., the glandular epithelium was destroyed at that point. The dentigerous tissue similarly grew with the cyst wall, and as in the case of the gland tissue, there were patches of degeneration due to stretching, &c., in which there were no teeth at all. It was therefore not surprising to see teeth in a teratoma $\frac{1}{2}$ in. away from another patch of teeth, and 3 in. or 4 in. away on the opposite side a third mass of teeth. The dentigerous tissue increased over a large area, and had the power of making involutions, and from those involutions teeth might arise, and did arise, except where the dentigerous tissue degenerated. Such was the latest theory, yet it was possible that sometimes cavities of reserve developed, so that a row of teeth represented, not independent involutions of the same age, but a genealogical series. Mr. Doran had with him a specimen of a formed tooth in its socket, with a crown below it, and what appeared to be a cavity of reserve, taken from the ovarian cyst of a young girl thirty years ago. The tooth was something like a bicuspid, and was socketed in a piece of alveolar tissue. Was that a tooth of a normal type with a true cavity of

reserve, or was Shattock's theory correct, that there were no cavities of reserve, but absolutely independent involutions?

Mr. MCADAM ECCLES said he would like to hear from members of the dental profession some suggestions as to why the teeth seemed to be more or less typical of the permanent dentition, and why they were so large in size.

Mr. F. J. BENNETT thought the point was that the teeth were developed once and for all, whereas the jaw might go on growing for years afterwards. The tooth took its form from the enamel organ, and the size was laid down at a very early age. Therefore, assuming the teeth were intended to form part of a normal being, they were exactly what would be expected. The tooth had arrived at a normal size, and remained the same though the surrounding parts might atrophy.

Mr. STANLEY MUMMERY asked Mr. Hopewell-Smith whether he had found any signs of erosion cavities in dermoid teeth. When studying erosion he was told by Professor Stewart that erosion cavities had been found in dermoid teeth. Such cases would be of special interest, as they rather militated against Professor Miller's theory of erosion.

Mr. HOPEWELL-SMITH said it was mentioned in the paper that Wedl described erosion of the teeth, but he himself had seen no evidence of erosion or caries.

Mr. MCADAM ECCLES, in reply, said that he was not quite sure whether he was right in saying that all caries was due to bacterial infection or action, but there was no doubt whatever that ovarian cysts might become infected with bacteria, and therefore there was a possibility of actual caries as the result of toxic infection in the dermoid cyst. Sometimes the infection of a dermoid cyst went on for a considerable length of time before it became necessary to remove the cyst.

The Complete Eruption into Place of a Devitalized Tooth.

By E. G. BETTS, M.R.C.S., L.D.S.

HAVING been requested to put on record the above case which occurred a good many years ago, I have looked up my notes and prepared the following: In June, 1884 (nearly twenty-eight years ago), a lady patient of about 25 or 30 years of age consulted me complaining of facial neuralgia on the right side, and that her plate no longer fitted comfortably. The plate had been made a few years earlier to supply two or three teeth and chiefly to remedy the loss of a temporary right upper canine which had persisted up to adult life but had then loosened

and fallen out. On examination I found that the plate, a small gold one, rocked a little, and on removal the cause was immediately evident. A tooth was present in the vacant space between lateral and premolar, and the point of its cusp, only just visible, was found to be carious, the cavity communicating with the pulp. No doubt it had rested against the gold for some time and thus had been more than usually exposed to decalcifying influences. In those days we had not pressure anæsthesia, so I applied arsenical acid, and in due course removed the pulp, filled the root, and inserted an oxyphosphate filling. The plate was cut away from the part involved, and when I next saw the patient about a year later the tooth had completely come down into place. I cannot, unfortunately, find the original model taken at the time, but the one I now pass round was taken a year or so ago and is practically the condition at present, except that a silicate filling now replaces the worn-down phosphate seen in the model.

The point of interest, of course, is the fact that the tooth has moved down the length of its crown without any assistance from the pulp, thus oversetting some theories of tooth eruption.

I may mention in connexion with this case another somewhat similar, where I found an exposed nerve under a flap of gum in a buried left lower wisdom tooth. This tooth being somewhat impacted, I devitalized and for the time treated with a temporary filling and some two years later removed without difficulty, it having in the meantime almost completely erupted.

DISCUSSION.

Professor KEITH hoped that the model would be presented to the odontological collection of specimens. He took it that the root was formed when it was in the jaw, so that it was a perfectly formed tooth.

Mr. BETTS said that was so; it was really a case of complete eruption.

Mr. JAMES said the case was of particular interest, having regard to the view accepted by many that all teeth of late eruption were due to the absorption of the tissue from above. The two neighbouring teeth standing as they did, and the tooth absolutely erupting into position, was remarkable at that age. It also affected the question in normal eruption of the growth of tissue carrying the tooth into position. The bone would undoubtedly be formed right up to the level of the necks of the neighbouring teeth. It would be of great interest to know the amount of bone formed in connexion with this tooth.

Odontological Section.

May 20, 1912.

Mr. H. LLOYD WILLIAMS, President of the Section, in the Chair.

An Unusual Case of Fracture of a Tooth.

By J. LEWIN PAYNE, M.R.C.S., L.D.S.

THE first of the two cases which I wish to refer to this evening occurred in a male, aged 45, who came to see Mr. Herbert Hooper, of Peterborough, complaining of neuralgia. Mr. Hooper could discover no dental cause for the trouble at the time, but when the patient returned a few months later he found an abscess in connexion with the right lower first premolar. The crown of the tooth appeared to be sound, but there was no thermal response, and he decided to open up the pulp. Notwithstanding the greatest care, he failed to locate the pulp cavity and discovered in the process of drilling that he had perforated the wall of the root. On the following day the pain was so severe that Mr. Hooper decided to extract the tooth, and he found the interesting specimen which I will now pass round (fig. 1).

You will observe that the tooth consists of two fragments, the crown and one-third of the root form one piece, and the lower two-thirds of the root form the other (fig. 2). Though quite detached, the upper part of the lower fragment is cone-shaped and fits accurately into the hollowed-out base of the crown portion of the tooth.

The specimen itself seems to indicate that the pulp chamber in the coronal portion has been completely obliterated by "secondary dentine," the skiagram (fig. 3) confirms this, and it is easy to understand why Mr. Hooper failed in his effort to reach the canal. The skiagram also shows that the pulp in the apical portion of the root remained uncalcified. Though there is no history to confirm my theory,

it seems probable that the tooth received an injury at some time during the calcification of the root, which, whilst sufficient to arrest development temporarily, and to separate the completed from the uncompleted portion of the tooth, was not enough to prevent the



FIG. 1.



FIG. 2.

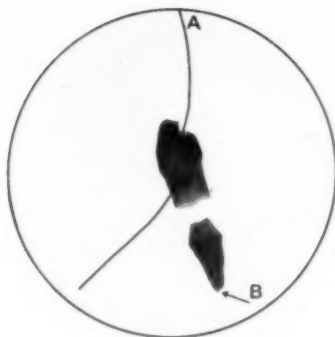


FIG. 3.

A, wire passing through opening in crown to perforation in wall of tooth.
B, apex showing pulp canal patent.

remnant of dental papilla from finishing its work. The formation of "secondary dentine" at the junction of the two fragments may be attributed to irritation. I have never seen anything quite like it before, and I shall be glad to hear the opinion of the members of this Section.

A Case of Acute Infective Periostitis.

By J. LEWIN PAYNE, M.R.C.S., L.D.S.

THE second case occurred in a lady who, in attempting to bite a hard lozenge, put considerable strain on her left lower central incisor which made the tooth slightly tender. The patient was in quite good health at the time, but about twenty-eight hours after the strain she remembers taking one or two spoonfuls of a milk soup which tasted putrid. By the morning of the second day she felt unwell and the pain and tenderness had increased. On examination, a few hours later, I found the tooth slightly loose and the pulp was dead, though up to the time of this strain the tooth had never given trouble nor was there any sign of caries. I should mention that the pulp of the adjoining left lateral incisor died about ten years previously, and the root canal had been treated and filled at the time and had given no trouble since.

The central incisor was opened up and the pulp removed but no pus came. After washing out the cavity a loose dressing of tricesol and formalin was inserted, and hot fomentations and counter-irritants were applied to the buccal sulcus. The pain, however, continued and became so acute that, on seeing the patient twenty-four hours later, I decided to extract the tooth. The apex of the tooth showed signs of commencing absorption. This was three days after the injury. For a time the symptoms improved, though the swelling did not entirely subside, but on the eighth day they had returned with increased severity, and the mischief began to spread with alarming rapidity from the original localized area of the left central incisor to the right side of the mandible as far as the first molar. Pain, tenderness, and swelling extended along the whole of the right side of the mandible. The patient was obviously ill, and had a temperature of 101° F. and a pulse of 98.

I consulted Mr. Tubby, who agreed that the case was one of acute infective periostitis, and we decided to sacrifice the right lower first molar whose pulp had been devitalized some five or six years before, and the left lower lateral incisor just referred to, the pulp of which had died previously. These teeth were extracted under an anæsthetic, and a deep incision was made in the sulcus between the symphysis and the right molar. This time, nearly 3 dr. of pus welled up, and a bacteriological examination revealed large numbers of a tiny streptococcus which at present has not been identified. No other

organisms were seen in a film of the pus. The cavity was packed with gauze and syringed out every four or five hours; considerable relief followed and the temperature quickly fell to 99.2° F., but two days later Mr. Tubby found it necessary to make a further incision to open up the whole area from the right second molar to the left lateral incisor, and from that time the condition gradually cleared up.

The nature of the infection and the rapidity with which the trouble spread are points of interest in this case. Upon careful examination of the teeth after extraction, I do not think there is sufficient reason to suspect either the left lower lateral incisor or the right lower molar as being responsible for the trouble, but when the mischief was spreading so rapidly we felt it wise to eliminate all possible sources of infection.

DISCUSSION.

Mr. J. G. TURNER said with regard to the second case, that if the onset of pain was due to sepsis from pyorrhœa there was no need to look for injury. He would like to know whether there was any history to lead to the supposition of a lowered vital resistance. He doubted the infection by the milk. It was as likely as not that the germ was there beforehand and obtained entry at the time of injury. It was possible that the dead nerve accounted for the putrid taste of the milk. The teeth and oral surfaces were covered with mucus, and the milk would have been more likely to upset the stomach than to infect a wound in the mouth, even an open wound, provided it was covered with its layer of mucus. The rapidity with which the disease spread was a thing very often seen, and sometimes the spreading took place down the throat, so that in a few hours the patient was in considerable danger. After the extraction of a tooth, when he thought he had been very careful in cleaning the mouth, he had seen a spreading down the throat and forward along the teeth, but he could not isolate any special germ. The presence of the small streptococcus was different from anything he had heard of before. He would like to know whether what he saw at the apex of the root of the incisor was an area of absorption, because that would probably mean that the tooth was infected before the injury.

Mr. W. W. JAMES thought the case was one of considerable interest. He had had a case fairly recently of a similar character, and he thought it was possible to get an infection spreading rather rapidly along the bone. Whether it spread along the bony canal or not it was difficult to say, but these cases seemed to occur in the front part of the mandible rather than in the larger area of spongy tissue farther back. In his own case there were two premolars with gold caps which the patient had worn with perfect comfort for many years, although he was unacquainted with the condition of the teeth beneath the caps. One day, however, she had acute pain, and apparently an infection

from the pulp cavity of one of the crowned teeth, which infection spread very rapidly indeed to the other side of the mouth as far as the first molar. There was not much swelling but intense pain, and the teeth were exceedingly tender. The two premolars were removed and a certain amount of relief was given. He found the canine on that side very sensitive to cold and dealt with its pulp, and more relief was experienced. But the inflammation persisted for some time, although further relief was given by means of fomentations and incisions. He had not seen another case so extensive as the one he had quoted. He had now a record of several cases where teeth had died, although free from caries or pyorrhœa, but where a neighbouring tooth was infected. Mr. Turner could probably recall a case at the hospital where a student complained of considerable pain in the region of the right maxillary incisors; an incision was made and the outer alveolar plate drilled high up over the apices of the roots, giving complete relief. There was distinct infection associated with the first premolar, and the pulps of the central incisor and lateral incisor were dead, although the teeth were perfectly good and free from caries. Since then he had made a point of collecting cases that apparently were due to infection from neighbouring teeth and had been able to collect several. It seemed quite possible in Mr. Payne's case that the tooth had been infected from its neighbour. Possibly the infection occurred, was of a very chronic character, and rendered acute by local disturbance. Infection from pyorrhœa seemed to be excluded, though it was rather difficult to exclude it sometimes, and he was quite sure that infection of a pulp could occur at the apical end of the tooth in the case of pyorrhœa.

Mr. H. BALDWIN said that possibly in Mr. Lewin Payne's case the left lateral incisor had died owing to a blow, possibly a slight one, in the front of the mouth, and possibly degenerative changes were set up by the same blow in the pulp of the central incisor. When the lateral incisor had its pulp extracted and the root filled, the central was probably alive, but may have died as the result of the same traumatism some time after. It would be interesting to know whether the pulp of the left central was found liquefied and decomposed or perfectly fresh. If it had been dead a long time it was probably the cause of the infection.

The PRESIDENT (Mr. H. Lloyd Williams) said that in many cases that spread very rapidly there was some previous history of illness, diarrhœa, or some other sign of infection, and he would like to know whether there was any such history in Mr. Payne's cases.

Mr. LEWIN PAYNE, in reply, referring to the second case, said there was no history of illness immediately preceding the onset of the trouble which would account for such an infection. The illness followed the slight injury of biting on a hard lozenge. A culture of the tiny streptococcus found, he believed, could be obtained from the bacteriological laboratory. With regard to the first case, he thought "pyorrhœa" did not enter into the matter. The point of interest was the unusual condition and the separation of the two halves of the tooth.

146 Schelling: *Extraction of Teeth from Newly Born Child*

Mr. J. G. TURNER said what he suggested was that the onset of the symptoms might have been due to pyorrhœa, not the actual infection.

Mr. PAYNE said he agreed that there had been periodontitis in both cases, but what Mr. Turner had said applied rather to the second than to the first case. The term "pyorrhœa" was being extended so as to apply to so many conditions that perhaps hardly three people in the room would agree as to its meaning, but surely Mr. Turner would not argue that it was responsible for the condition of the first specimen he showed. With regard to the question of Mr. Baldwin, concerning the lower lateral incisor in the second case, there was no history of trauma. The death of the pulp occurred insidiously, giving rise to pain and acute inflammation without previous history of injury. He was of opinion that the pulp of the central incisor had only recently become devitalized, because at the time of extirpation it came away practically complete.

Extraction of Teeth from a Newly Born Child.

By CARL SCHELLING, L.D.S.

EARLY this year Dr. Robert D. Muir, of New Cross, asked me to see a newly born baby with teeth. I went down the same evening and saw a healthy little girl with two lower temporary incisors in position. The mother was most desirous of nursing this, her first, child, and as she refused to make use of a nipple-shield I was asked to remove the two teeth, which I did, after taking an impression in composition of the lower jaw. The first extraction was attempted with a small lower hawk's-bill forceps, and the crown of the tooth collapsed and came away, leaving a papilla containing many sharp spicules of calcified tissue; this I removed. The second tooth I grasped lightly with a straight upper incisor forceps and used a rotatory motion, and this tooth came away without altering its shape. The mother was greatly pleased at being able to nurse her child without pain. I pass round the model and teeth, and though, like the classical case of King Richard III, many cases of children born with teeth have been recorded, yet they cannot be common, as one of the most celebrated London accoucheurs informed me that though, of course, he had heard of such cases, yet he had never seen one himself. I must admit that I felt considerable apprehension lest I should tear the gum, as the teeth, though not implanted in sockets, were strongly adherent.

DISCUSSION.

The PRESIDENT thought the impression shown was one taken from the youngest person he had ever seen and congratulated Mr. Schelling on taking the impression.

Mr. J. G. TURNER exhibited the model of a similar condition; the child was born with a lower central erupted. The tooth was only a partly formed crown and fell out in a few days. He had the model of a child born with two lower central incisors and at the age of fourteen the teeth were still there; so that they did not always fall out. The teeth often were mere shells. He had hitherto failed to obtain a history of what happened afterwards—whether the child had any further teeth in those positions after the shells had been thrown off. He thought that in some cases there was no doubt that it was a matter of syphilitic necrosis; but the history was very difficult to get. He hoped that Mr. Schelling had taken microscopic sections of the papilla as it might help to throw some light on the question of eruption.

Mr. C. SCHELLING said that after he had taken the first tooth out he noticed that a papilla remained containing sharp spicules, and he removed it to the level of the gum.

A Case of Arrested Eruption of the Teeth associated with Arrested Development of the Mandible.

By A. T. PITTS, M.R.C.S., L.D.S.

THE patient in whom this condition was found was a young man aged 23. He was quite healthy and well developed, except in regard to the lower jaw. On examining his mouth it was seen that the only teeth that were in occlusion were the incisors and canines on the right side, one upper and two lower premolars.

4	3	2	1		1	2		
5	4	3	2	1		1	2	3

The lower incisors were a little in advance of the upper, probably a bite of accommodation. On the left side in the mandible the first premolar was apparently missing, the second premolar and the first and second molars were present, but the crowns were only just exposed, and looked inwards. In the maxilla there was an ill-fitting bridge apparently over the first premolar and first molar, so that it was not possible to estimate the amount of eruption of those teeth; the second molar was normally developed. When the mouth was closed there was a space between

upper and lower cheek teeth of $\frac{3}{8}$ in. at the widest part. On the right side the first lower molar was badly carious, but sufficient of the crown remained to show that it was only imperfectly erupted. In the maxilla the premolar and first molar were normal, while the second molar was only just erupting. There was no history of any severe illness as a child. The patient stated that the teeth had remained stationary, certainly for some years.

The jaws were then skiagraphed, and on examining the plates it will be seen that the patient has his full complement of teeth. All four third molars are present, also the left first mandibular premolar and the second left maxillary premolar. Just behind the latter tooth is a small calcified mass, somewhat irregular in form, but without any root; I am



Right side.

FIG. 1.

Left side.

Models showing lack of occlusion of molar teeth.

not sure whether it is a supernumerary tooth or a portion of a deciduous tooth. If you look at the body of the lower jaw you will see that anteriorly, where the incisors and canines are fully erupted, the bone is normal in depth; but laterally it is very different. The compact bone is greatly reduced in depth; while the mandibular canal appears to be in contact with the lower border. There is practically no bone intervening between the roots of the molar teeth and the layer of compact bone, whilst the most superficial portion of the alveolus around the necks of the teeth seems to be much denser than usual.

Concerning the ætiology of this case I am afraid I cannot offer any suggestion. For some reason the body of the jaw laterally has ceased to grow properly and, as a consequence, the molar and premolar teeth,

although fully formed both in regard to their roots and to the alveolus forming their sockets, have not erupted properly. The case would suggest that the eruption of the teeth is dependent upon the growth of the bone beneath the tooth, and where the growth is absent neither the completion of the root nor the growth of the alveolus around the tooth is sufficient to cause the eruption of the tooth.



FIG. 2.

Skiagram of mandible.

DISCUSSION.

Mr. JAMES asked whether the patient had any habit of putting the tongue on that side of the mouth, because he had seen marked deformity produced by tongue-sucking and biting of the tongue on one side. He had two patients (sisters), now at the Royal Dental Hospital, who were considerably deformed on one side through sucking the tongue, and the bite was greatly opened. It was quite possible if the tongue was large that it might produce the condition, although it was hardly probable.

Mr. PITTS said he did not make any inquiries as to habits, but he would scarcely imagine that the habit referred to could produce so marked a deformity as he had shown, although he was well aware of the amount of deformity that could be caused by habits.

A Simple Apparatus for Prevention of Laceration of the Tongue during Sleep by Spasmodic Closing of the Jaws.

By ASHLEY DENSHAM, M.R.C.S., L.D.S.

I VENTURE under the circumstances to bring forward this simple device for the alleviation of a condition which causes considerable suffering to some people. I have never noticed any reference to it in literature, and I thought it would be interesting to find out whether the other members of the Section had come across similar cases. This apparatus was devised because the patient complained that he frequently lacerated his tongue severely at night. Whenever he slept on his back he had such violent spasmodic contractions of his jaw muscles snapping the teeth together that he lacerated the tip of his tongue to the extent that on occasions there was considerable hæmorrhage, and blood on the pillow in the morning. It got on his nerves to such a degree that he developed insomnia, so terrified was he at the idea of falling asleep and biting his tongue in this way. I had not come across a similar condition and I was rather nonplussed as to what to advise him to do. I suggested several things and tried one or two things, and then we hit upon this simple device, which consists of an india-rubber macintosh pad perforated for breathing, shaped like the old-fashioned "respirator," with a projection at right angles to it. It is worn with the projection between the incisor teeth and the strings are tied round the head and above the ears. He kindly provided me with this one which he has worn for some considerable time, and it shows what tremendous force his jaws exercised, because what might be called the teat is absolutely severed from the pad and is mended for exhibition purposes with cotton. It is a cumbrous thing, and my impression is that it might be made much smaller and still be efficient, but the principle of the thing is simplicity itself, and he says it has made the whole difference to his life; he can now go to sleep in full consciousness that he will not bite his tongue. My attention having been drawn to that condition, I soon afterwards found there were other people suffering from the same complaint. He has now worn the apparatus for some two years, and still finds that if by any chance, being away from home, he has forgotten to take it, the tongue suffers severely in the old way. The trouble is therefore not cured but only alleviated.

As far as I can gather, the people who are inclined to this condition are people who suffer from brain fag. The first patient was a clergyman in a large parish, the second a schoolmaster, and the third a barrister in a busy practice. They all complained of the fear of going to sleep, and the considerable laceration of the tongue, and they all expressed very great gratitude at the relief given by this device. I thought if any other members of the Section had patients who were suffering from a similar condition they might be grateful to have this matter brought to their notice.

DISCUSSION.

Mr. W. RUSHTON said he had had a similar experience in a patient who bit the tip of the tongue in going to sleep and made it very sore. The difficulty was got over by making him a strengthened vulcanite plate to cap the molars, and so prop open the bite at night, and it seemed a much simpler thing than Mr. Densham had shown, although perhaps the cases were not analogous.

Mr. CARL SCHELLING said he had a patient who, if he slept on one side, woke in the morning with great pain in the tongue, which, by its own weight, used to find its way between the upper and lower jaws and get bitten. He made a plate somewhat like that described by Mr. Rushton and it was effective, but the patient was afraid of swallowing it, and to prevent that he had a piece of fishing-line attached to the plate and tied to a button. After wearing it for some time he was able to give up the habit and now slept without the plate.

Mr. DOUGLAS GABELL said he had a case of grinding the teeth together at night, causing great distress to the patient and to the patient's wife, as she was unable to sleep on account of the noise. He made a soft rubber denture to cover the lower teeth and articulate with the upper ones, stopping just short of the lower gum, so that there was no uncleanness round the necks of the teeth. It was difficult to get a nice smooth finish on both surfaces. A hole was bored through the denture and it was tied to the patient's pyjamas at night. It served its purpose so efficiently that in the daytime he could sit in a chair, slip the machine in, and immediately go to sleep.

Mr. DENSHAM, in reply, said he had tried Mr. Rushton's idea of capping the molars with vulcanite, but the patient bit through the vulcanite very soon and was constantly swallowing small bits of it.

A Few Notes on Porcelain Work.

By DOUGLAS GABELL, M.R.C.S., L.D.S.

THE method I propose first to describe is that of making continuous gum blocks, joining six or more teeth together with porcelain to fit on to gold or vulcanite plates, without the use of a platinum base. My method has been to set up the teeth on the model and then take an ordinary overcast of the front to get a register of where the teeth happen to be, and I then cut away the wax from the back, leaving just sufficient for the proper thickness of porcelain. Into the back thus prepared I pack Price's artificial stone, which I find a useful material for standing very great heat. The stone has to be heated to a red heat to get it hard. I then take the stone and soak it with wax. If porcelain is packed direct on to the stone and then fused it will adhere so tightly that grinding is the only method of separating them afterwards. Then I reset the teeth on the artificial stone by fixing them at the back with little pieces of hard wax, and replace the gum in front with ordinary wax to get the contour I require. Then I take the little blow-pipe used for hollowing out cast gold inlays and make holes all over the wax. That has a twofold object. I can get little pieces of porcelain separate and allow them to shrink without any hindrance and thereby obtain much greater strength, and also by sucking out the wax in that way I can determine the exact thickness of my porcelain all over the area of the gum restoration. In my early attempts I found it very difficult to get an even thickness of porcelain all over. By this method I get out the wax and then fill all the little 'honeycomb' holes with porcelain. I put it into the furnace and pack it round with silex to keep the teeth from being thrown out of position. I have used a piece of an old crucible to make a little box into which I could pack the thing tightly and prevent any movement of the teeth. When it comes out fused each tooth is separate and each piece of porcelain is separate, each having shrunk on itself without any hindrance, and therefore has the maximum strength. The stone is re-waxed and all the little pieces are put together again and the crevices filled in with the porcelain and it is again fused. The crevices being small there is very little shrinkage and I can get a very good fit. When it comes out again it may be necessary to put it in once more to remedy any little error. The gum body is put

on last. Thus I can get the teeth fixed together with a gum body of the thickness, contour and accuracy I desire. I used at first to fuse the gum body and get a nice shiny surface, but I found that an under-fused surface, a granular, rather poor looking surface out of the mouth looked very much more natural in the mouth.

For the specimens I have shown you I have used diatoric teeth. Such teeth make decidedly weak blocks on account of the large dovetails between each tooth. With Dowell crowns you can put porcelain at the back and make it much stronger. All the specimens I have passed round have been done by a two-year pupil, so you must not be too hypercritical as to the workmanship. The plate I am passing round was set up with tube teeth which were fitted not very accurately and then all waxed together, the front six teeth and the four side teeth each forming one block. Teeth and wax were lifted off in one piece and an artificial stone base prepared for each piece. Then the porcelain was packed in between the different teeth and a cut made right through between the tube teeth to allow of shrinkage, or during the first fusing they will draw together and not go back on to the plate. They were filled in between in the second fusing and the side blocks had no fitting done afterwards. There has been no shrinkage at all. A little trouble I had was that when I got thin edges of porcelain it was very difficult to get them to fit accurately. In the piece going round you will notice that the one with the gum enamel has the edge curled up a little on the outer side, whereas the one without the gum enamel is fitting very well indeed. Those are fitted on to a gold plate and when I get that turned-up edge it is a difficult matter to get the joint nicely. If you put more gum on it goes up to a round edge. A little dodge I have to get over it is this: I grind the edge to a distinct opening; then I pack the joint between the gold plate and the porcelain with Alexander's plastic gold—ordinary moss gold with a certain amount of paraffin wax mixed in it to make it work nicely. Then I take off the porcelain block, invest the plate and gold in the plaster and pumice investment and run in solder so as to get a thin gold edge and thick porcelain edge which will fit perfectly. When doing porcelain work with a gold base I have very little trouble with it, but when I use vulcanite there is considerable difficulty. Coming out of the vulcanizing process they generally are cracked, or if they come out sound and are put aside they crack two or three days or even a week afterwards. It has been suggested that I should heat the blocks when they come out of the vulcanizer to allow a little contraction at the back to take place, but I have not had time to test this.

I have introduced this method to you to-night because I thought it would be of interest, as an article has appeared in a journal describing the making of six tooth gum blocks as an entirely new invention, when as a matter of fact a good many of these were shown last October at the Royal Dental Hospital, and the pupils do the work as part of their regular course.

DISCUSSION.

The PRESIDENT said he had been acquainted with the difficulty of continuous gum blocks cracking for a very long time, and he had never been able to satisfy himself as to the cause. No doubt it was quite a common thing. Sometimes there was success in getting the block out of the vulcanizer without a crack, and yet before it had left the workroom a crack had developed. If the block had been in the mouth one would have been inclined to say it was due to strain. The first cracking of a block he had seen had taken place very soon after the patient had commenced to wear the case, and he thought the patient must be to blame, but when he found later that cracking took place before the patient had worn the denture, he had to review the matter altogether. The method of getting small mosaic bits of porcelain work was an extremely clever one, and he had already had an opportunity of congratulating Mr. Gabell on it last October. He thought Mr. Gabell would agree that at the present time what he had to say was not entirely encouraging from the point of view of the method becoming common in the workroom, but with his usual persistence and industry no doubt he would develop before long some simple method of doing the work.

Mr. GABELL, in reply, said that the fact that the blocks broke before they had any strain in the mouth was perfectly true. At first he was much surprised and very sceptical, thinking they had been mishandled, but it was really a very old trouble. Looking back to the literature of the subject, he had found that many men had succeeded in making blocks, but no one had yet succeeded in vulcanizing them safely. With regard to the simplicity of the work, a block of six front teeth in vulcanized plates required great neatness, cleanliness, and exactitude. With regard to fixing tube teeth together and mounting them on gold pins or mounting Dowell teeth on gold pins, that was now quite a simple process and could be done by any moderately careful worker. It had the great advantage of being cleanly and overcoming the only objection he had ever heard against tube work, that it was uncleanly. He always fused the gum enamel more extensively at the back of the mouth, because there it was not beauty that was required, but a self-cleansing surface. He had never yet met any surface equal to porcelain for keeping clean in the mouth.

Odontological Section.

June 24, 1912.

Mr. H. LLOYD WILLIAMS, President of the Section, in the Chair.

Some Pathological Conditions found in the Teeth and Jaws of Maori Skulls in New Zealand.

By H. P. PICKERILL, M.D., M.D.S. (New Zealand).

I HAVE had occasion during the last few years to examine some hundreds of Maori skulls in this country, and during the course of my investigation have observed several pathological conditions (other than caries); some of the cases seemed sufficiently interesting to photograph and record. As regards caries of the teeth, as I have stated elsewhere,¹ my observations place the incidence of caries in the Maori race at a lower figure than Mummery's, namely, at 0.76 per cent., this being even lower than Mummery's figures for the Esquimaux, and if the two may be compared, then the Maori was more immune to caries than any other race.

ATTRITION.

All Maori skulls show marked attrition of the teeth; this is, as a rule, very uniform, but is more marked on the first molar than on other teeth. Even in the skulls of children of the age of 12 to 14 the cusps of the first molars are, as a rule, quite worn down. Fig. 1 illustrates a typical Maori dentition of about middle life. The "edge-to-edge bite" is of course acquired and is directly due to the attrition. The lower jaw

¹ "Prevention of Dental Caries and Oral Sepsis."

has moved upwards and slightly forwards through the segment of its normal curve of movement, and the lower margin of the upper incisors has through attrition retreated slightly by reason of the backward inclination of the upper part of the crown. In the majority of cases attrition has been attended by the formation of adventitious dentine in the pulp chambers; thus although the teeth are worn down



FIG. 1.

Maori skull, showing typical dentition—i.e., excessive attrition. In the majority of teeth the pulp chamber becomes occluded by adventitious dentine. The "edge-to-edge bite" is, I believe, not normal, but acquired as a result of the attrition.

far below the original level of the pulp, the latter is perfectly occluded by the apparently hyaline variety of adventitious dentine. In many instances the secondary deposit is so translucent that a cavity seems to be present, and it is only on using a probe that one realizes that it is a hard, smooth, glassy surface. In some cases, however, attrition has

overtaken repair and then the pulp chamber has been laid open, leading to the inevitable result—the formation of alveolar abscesses. Thus although the Maori was undoubtedly very free from dental caries, "toothache" was by no means unknown, and he must have experienced all three of the primary forms—i.e., that due to myelitis, periodontitis, and alveolar abscess. Fig. 2 is a photograph of a skull showing multiple alveolar abscesses developed in this way. This particular individual

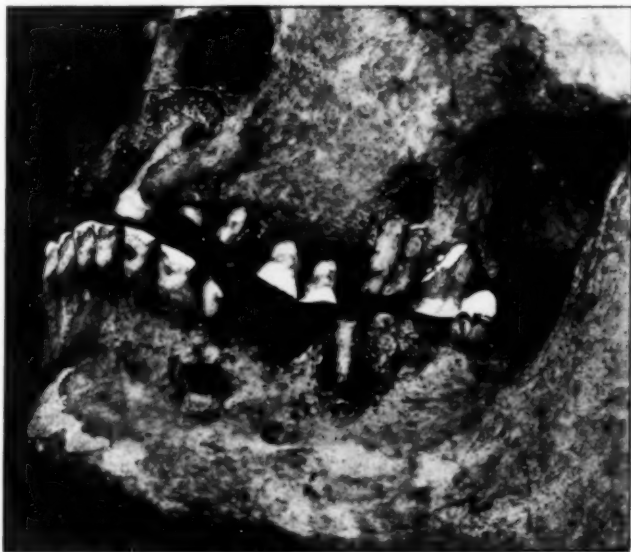


FIG. 2.

Maori skull, showing multiple alveolar abscesses. This condition was common amongst the Maoris and occurred in those teeth in which adventitious dentine failed to occlude the pulp chamber. Note the abscess cavities at the roots of the upper central incisor, lower premolar, lower first molar and upper first molar, the latter invading the antrum.

must also have suffered from empyema of the antrum, since one of the abscess cavities communicates freely with the sinus.

It is popularly supposed that the extreme attrition of the Maori's teeth was due to a coarse and gritty diet, but I am convinced from inquiries on this point that this is very much over-estimated. As I have shown at length elsewhere (*loc. cit.*), the Maori took extreme care in

eliminating the fibrous elements from his food, and the cooking was prolonged and by the earth oven or steaming process. Some food was kept in this process for seven days, and my colleague, Professor Marshall, who has quite recently eaten food prepared by the Maoris in this latter way, informs me that he never tasted more tender or better flavoured food in his life. Maize they steep in water in the open for a prolonged period until it is very "highly" flavoured indeed. The attrition is due, I think, to a combination of a slightly fibrous diet combined with the acids of fruits and berries, the evidence in support of which would be too lengthy to introduce here.

DISLOCATION OF THE FIRST MOLARS.

I am not aware that this peculiar form of dislocation has been noted before in the skulls of other native races or an explanation offered from a dental point of view. In a number of skulls (I regret to say I did not keep a precise record since these were merely observations by the way) both upper and lower molars were found to be dislocated inwards towards the middle line, and in some cases to be lying horizontally in the jaw, and to have been so worn by attrition that a complete "section" of the pulp chamber and root canals is visible (fig. 3). Dislocations in all stages are found, from a just perceptible inward tilting to complete loss of the tooth; in the latter cases, from the condition of the alveolus and the position of the socket of the palatine root—i.e., well towards the buccal side of the alveolus—it is obvious that dislocation has been complete (*see* figs. 4, 5). I think the condition is to be explained as follows: All the teeth subject to the dislocation have had the pulp chamber opened up through attrition, and the subsequent alveolar abscesses have destroyed a portion of the external alveolar plate, thus considerably weakening it. The individual would in this condition have a chronic alveolar abscess with frequent intermittent attacks of subacute periodontitis. To relieve the pain of the latter condition he would grind his teeth together or perhaps bite on some hard substance. (Inquiries on this latter point have, however, so far been negative.) Now I believe from subjective and objective experience that such pressure is naturally brought to bear on the offending tooth by the lower jaw being thrust outwards on the affected side and then drawn forcibly upwards and inwards. In the same direction, too, pressure is normally applied in the mastication of ordinary articles of diet—that is to say, in the mastication of food on the right side the

pressure is applied from below upwards and inwards towards the middle line. The result of this will be, bearing in mind the loss of the external alveolar plates, that the palatal side of the upper molar is tilting upwards and inwards. This throws the brunt of the masticating force on to the buccal cusps area of the lower molar, and therefore also subsequently tends to thrust that tooth inwards and downwards. The conditions once being established would tend to get rapidly worse when the lines of force fell within the margins of the internal alveolar plates (*see fig. 6*). In support of this theory is the fact that when the formation of adventitious dentine has kept pace with attrition, and



FIG. 3.

Maori skull, showing attrition of teeth resembling "the mark" on the horse's teeth. The first molars were occasionally worn to the pulp chamber before the second molars erupted, and were but rarely occluded by adventitious dentine; resulting in the destruction of the buccal alveolar plate by alveolar abscesses.

therefore no destruction of alveolus taken place, no dislocation is present, although the tooth may show very considerable attrition.

A few skulls showed evidence of general osteoporosis of the alveolar bone, due presumably to the condition commonly called "pyorrhœa alveolaris" (but which I prefer to term a septic arthritis). Fig. 7 is a good example of this. I am not sure, however, that a suppurative gingivitis may not have been more common than would appear from the evidence of the skulls. The Maoris evidently recognized some such condition and also the necessity of guarding against contamination and

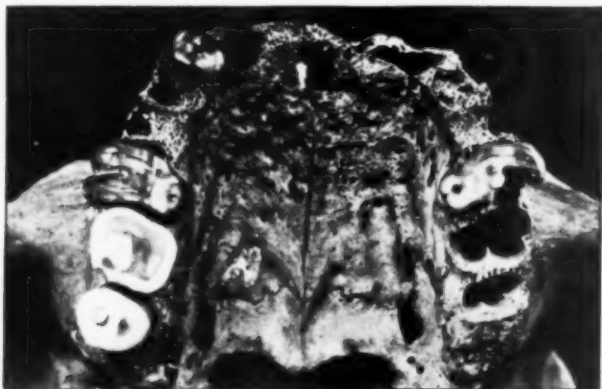


FIG. 4.

Maori skull, showing bilateral inward dislocation of first molars. This condition is found occasionally. The grinding in such cases is most powerfully applied in an inward and upward direction for the upper teeth, and downward and inward in the lower teeth. Thus the internal alveolar plate acts as a fulcrum around which the tooth rotates.

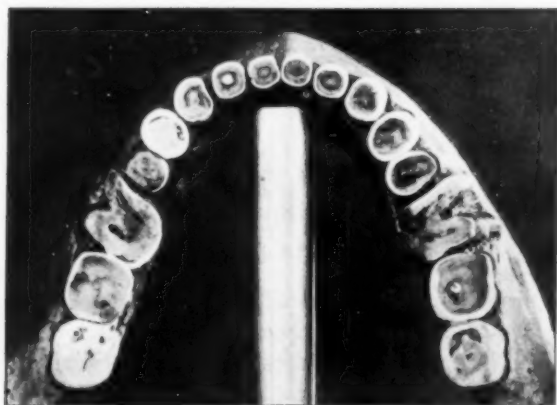


FIG. 5.

Maori jaw; bilateral inward dislocation of first molars showing a similar condition in the lower jaw. The surfaces are beautifully polished and show in some cases a complete section of the pulp canals. Possibly the Maoris used a piece of greenstone for biting on to relieve the chronic periodontitis.

infection from such a source, as may be gathered from the following notes obtained from the Maoris themselves:—

“Very few persons (Maori) were afflicted with toothache, and steps were taken to banish the tunga (grub), which was got rid of. All food baskets, water vessels and food vessels used by elderly persons afflicted with niho tungo (toothache) were used by them alone. All younger folk not so afflicted used separate vessels. Hence the soundness of the teeth of the Maori, and hence, by such care, toothache was confined to very few. Another reason why our elders and ancestors had such good teeth is their excellent modes of cooking, steaming and roasting only, and no food was eaten very hot. Hence the soundness of their teeth and their general healthy condition. (The Maori believes that tooth-

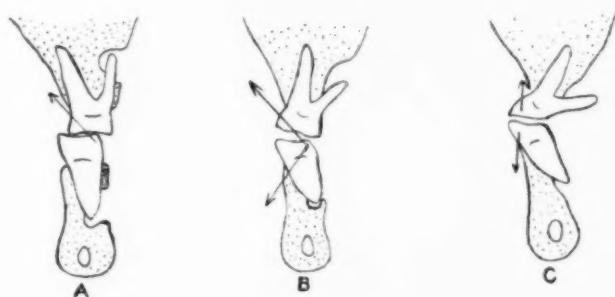


FIG. 6.

Diagrams representing stages in the dislocation of the first molars. **A**, primary stage of unstable equilibrium due to loss of buccal resistance; **B**, initial tilting of molars causing lines of stress during grinding, to pass outside the alveolus; **C**, stage when very little stress on the lingual halves of the occlusal surfaces will cause considerable rotation.

ache is caused by a grub (tunga) in the tooth, hence term ‘niho tungo,’ and hence, also, above precautions).”

“The resinous heart wood of the rimu tree (*Kapara rimu*) was used as a tooth powder. A piece of this heart wood was pounded until so crushed that a certain amount of dust-like matter resulted. This was put in a shell and mixed with water. This dust-like matter was termed ‘pungarehu Kapara,’ by some ‘nehu Kapara.’ When the teeth became discoloured with dark stains, as sometimes seen near the gums, the above mixture was used to cleanse them. The finger was dipped into

the mixture and rubbed on the teeth. This discoloration of the teeth is termed 'taiakiaki.'

One skull showed extensive loss of alveolar bone, which may have been due to extensive osteoporosis following general septic arthritis, or more probably to necrosis during tertiary syphilis, which unfortunately was introduced very early by the whalers (fig. 8). Another figure shows a somewhat similar condition in the lower jaw when the very



FIG. 7.

Maori skull, showing excessive absorption of the alveolus in the incisor region (upper and lower jaw) probably the result of "pyorrhea alveolaris." The condition was extremely uncommon.

superficial position of the mental foramen is well seen. Had this individual been so unfortunate as to be afflicted with an artificial denture, I am afraid a considerable amount of neuralgia would have resulted. And even without the denture pain was probably not entirely absent during mastication.

Complete disorganization of the temporo-maxillary joint was seen in one skull (fig. 9). The condyle has completely disappeared, and also a considerable portion of the angle. The ascending ramus is very much thickened and at the same time traversed by many superficial sinus tracks. It would seem not improbable that the origin of the condition was some traumatism which became infected possibly by some such organism as the *Streptothrix actinomyces*.



FIG. 8.

Maori skull; anterior view. The skull does not show any signs of very advanced age.

Dilaceration and non-eruption of a canine tooth was observed in a Maori skull. This individual must have suffered considerably, since both the bone and the tooth show ample signs of rarefying osteitis, and sinuses open on to the palate, into the buccal sulcus and also into the antrum.

Finally, I was much surprised at the frequency with which the third molars were suppressed or unerupted, and this point is, I find, illustrated in some of the accompanying photographs. It is not uncommonly stated that the suppression of the third molar is an

accompaniment of advanced civilization and represents a stage in the evolution of the human jaws. But how can this be reconciled with their so frequent absence in such a race as the Maori? For the Maoris were, and are now in some parts, physically excellent, with fine, broad, well-developed dental arches, and with no obvious reason for the absence of the wisdom teeth.

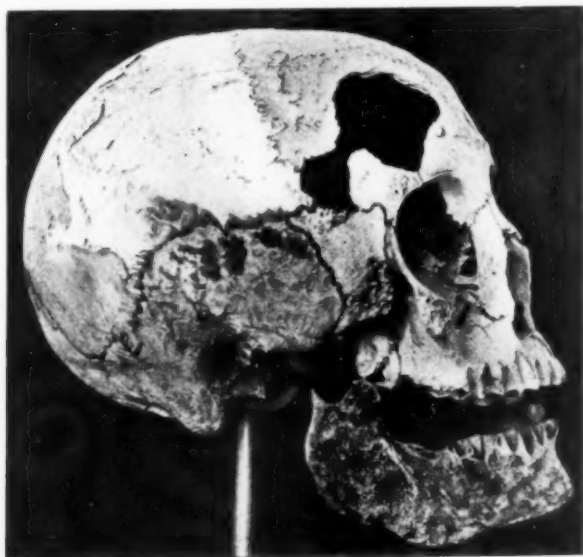


FIG. 9.

Maori skull, showing extensive necrosis of the lower jaw (vertical ramus and angle). The condyle has disappeared and the glenoid fossa is disorganized. Probably arose from a traumatism which became infected by chronic disease (such as actinomycosis).

Another interesting problem raised by the foregoing cases is the extent to which the owners of the jaws and skulls may possibly have suffered in the flesh from the systemic effects of "oral sepsis."

DISCUSSION.

Mr. W. RUSHTON did not think the author should take it for granted that an edge-to-edge bite in the skull exhibited was the result of attrition. In many primitive cases the edge-to-edge bite was a normal one, and the opinion had been expressed by Professor Keith, of the Royal College of Surgeons, that it was the bite of primitive man. Some little time ago he himself had brought to the Section a case of painful attrition with tremendous wearing down of the molars, and in that case the bite was not edge-to-edge, but the lingual portion of the upper incisors were worn down. With regard to the skull which was shown as an example of pyorrhœa, he thought that in specimens of that kind the age of the individual should be given. It should not be forgotten that Nature's method of getting rid of teeth in old age was by the absorption of the alveolus which supported them and a consequent loosening of the teeth.

Mr. W. W. JAMES thought it should hardly pass without question that the displacement of the first molars could be due to the exposure and infection of the pulp of the tooth with the sequence suggested by the author. If the exposure were due to attrition it might be expected that other teeth would be affected similarly. He would like to know whether any habit of the natives could cause such a displacement. The dislocation of the tooth in the manner depicted was certainly extraordinary.

Mr. WHITEHOUSE, referring to the remark of the author that food was not taken into the mouth at too great a heat, said that in the "History of Dental Surgery" from 1771 to 1826, the early writers, following John Hunter's work, laid very great stress upon the fact that food should not be taken into the mouth too hot, as it was thought to be the cause of caries before the theory of micro-organisms was put forward. It was curious that if this were an expression of opinion by a native, that it should coincide with the very earliest teachers of dental surgery—Fox, Bell, Robertson, and others.

The Nerve Supply of the Dentine.

By J. HOWARD MUMMERY, M.R.C.S., L.D.S.

IN March, 1911, I communicated to this Section¹ a short note on the nerves of the dental pulp, describing the results of a fresh examination of some specimens prepared some twenty years ago which seemed to indicate that the ultimate nerve-fibres of the pulp entered the dentine. In the year 1892 I had seen clear indications that the nerve-fibrils did not terminate at the inner margin of the dentine, but by the method I then employed I could not succeed in making this sufficiently clear for a conclusive demonstration. During the last year I have made a very extensive investigation of fresh material, treated by many different methods, and the results were embodied in a communication to the Royal Society in February last, and were lately published in the *Philosophical Transactions*.² I am exhibiting under the microscope this evening a series of preparations which will I hope make it evident to you that my views concerning the distribution of the nerves of the dental pulp are fully confirmed by the results of this further investigation.

It may be well to introduce the subject by reminding you of some details in the microscopical anatomy of the sensory nerves of the body generally, and for the sake of comparison draw attention to their mode of distribution in various tissues. Nerve-fibres arise from nerve-cells, and the central part of the nerve-fibre, the axis cylinder, is a prolongation of a process present in all nerve-cells called the "axon" of the cell. A fibre of the axis cylinder is continuous throughout its whole length from cell to final distribution. The nerve-fibres of the sympathetic system consist entirely of a prolongation of this axon, but other nerve-fibres are enclosed to within a short distance of their peripheral distribution by a surrounding sheath of a fatty material which stains black with osmic acid, and is called the medullary sheath; and also by a membranous sheath external to this, containing nuclei and called the neurolemma or nucleated sheath of Schwann. The neurolemma is constricted at intervals by what appears to be a narrow band, the constriction of Ranvier, and the medullary sheath is interrupted at these

¹ *Proceedings*, 1911, iv, pp. 51-56.

² *Phil. Trans. Roy. Soc., Lond.*, 1912, B, cclii, pp. 337-49.

nodes or points of constriction, the axis cylinder passing uninterruptedly across the intervals. This continuous axis cylinder is the essential and most important part of the nerve-fibre, and as the fibre nears its final distribution the axis cylinder loses, first, its neurolemma or fibrous sheath, then its medullary sheath, and finally divides into innumerable fine fibrils, the neurofibrils or ultimate elements of the nerve-fibre. We thus see that the axis cylinder which is the direct prolongation of the axon of a nerve-cell leaves the cell as a naked bundle of neurofibrils embedded in a homogeneous matrix; it acquires a sheath or sheaths which serve to protect it in its course through the tissues, and finally loses its sheath and is again a similar bundle of neurofibrils in a similar homogeneous matrix. At their final distribution there is, according to Schäfer, abundant evidence of the branching and reunion of the neurofibril.

It is considered that these fine fibrils are of a semi-fluid nature, as under the action of reagents they become varicose or beaded, as if they were of a viscous nature and not solid. This beading of the neurofibrils appears to be much more evident when they are subjected to the prolonged action of reagents in the preparation of sections. The conducting substance of nerve-fibre is considered by Carlson and others [28] to be necessarily fluid.

Treating of the afferent or sensory nerves I would like to draw attention to that mode of termination of nerves which consists in fine ramifications of the axis cylinder passing between the elements of the tissues. In these instances, the medullated nerve, after frequent branching, loses its medullary sheath and the fibrous sheath or neurolemma, and is continued as the axis cylinder only, which is made up of fine beaded fibres—the neurofibrils. These fine fibrils enter into a plexus, which is a fine interlacement of neurofibrils, but probably not a true network in the sense of an anastomosis, the fibres, although giving off branches and minute subdivisions, remaining quite distinct from one another. In epithelia this mode of termination is especially evident, being seen in the skin and mucous membranes, the cornea and serous membranes. The fine fibrils in these situations may either end in flattened expansions or in minute, very delicate, fine-beaded fibrils. In the epithelium of the cornea they are seen to terminate in very delicate varicose fibrils.

In describing free nerve-endings in epithelium, Professor Schäfer speaks of the neurofibrils as forming a primary plexus from which small branches are given off to a secondary plexus nearer the surface, and

from this latter plexus nerve-fibres proceed to form terminal ramifications among the tissue-cells. This is the mode of termination I have described in the human tooth and to which I shall presently refer. In many instances the neurofibrils end in small expansions and knob-like bodies, sometimes in loops, and sometimes, as in the cutis vera, in small flattened bodies like leaves—called by Ranvier, hederiform nerve-endings.

It is very remarkable that for a long period it was considered that dentine is not sensitive, and even such a great authority as John Hunter [10] was of this opinion, for he says: "The teeth would seem to be very sensible, for they appear to be subject to great pain, and are easily and quickly affected by either heat or cold. We may presume that the bony substance itself is not capable of conveying sensations to the mind, because it is worn down in mastication and occasionally worked upon by operators in living bodies, without giving any sensation of pain in the part itself. In the cavity of a tooth (i.e., the pulp) it is well known that there is exquisite sensibility, and it is likewise believed that this is owing to the nerve in that cavity. This nerve would seem to be more sensible than nerves are in common, as we do not observe the same violent effects from any other nerve in the body being exposed either by wound or by sore, as we do from the exposure of a nerve of the tooth. Perhaps the reason of this intenseness, as well as the quickness of the sensation of heat and cold in the teeth, may be owing to their communicating these to the nerve sooner than in any other part of the body." The editor, in a footnote, says, writing in the year 1837: "That the bony substance of the teeth is itself capable of conveying sensation to the mind is, notwithstanding the author's assumption to the contrary, easily proved. Whence otherwise arises that acute sensation so commonly felt when the neck of the tooth is touched with the nail, or with any sharp instrument, or when a portion of the enamel only is broken from the surface of a tooth."

Duval [2] showed in a paper which he read before the Academy of Medicine in Paris in 1831 that there is sensation in the dentine and was of opinion that it is chiefly manifested just beneath the enamel.

Salter [24], in his classical work on "Dental Pathology," writing in 1874, says: "The nerves of the tooth pulp form loops towards the periphery which may be readily demonstrated by the action of caustic alkali, and from these, according to Boll, large numbers of very minute fibrils proceed outwards, passing between the ivory cells and their tubular prolongations. It is highly probable that these are the nervous elements

distributed to the dentine, but whether they pass into the intertubular substance, or, fastening upon the tube walls, are so piloted into the ivory structure, is quite uncertain. It is, however, highly improbable that they pierce the wall of the ivory cell and occupy the axis of the tubes."

Boll's observations [1] were made in 1868, on the teeth of rodents which he treated with a very weak solution of chromic acid ($\frac{1}{16}$ to $\frac{1}{32}$ per cent.). His preparations showed fine fibres in great abundance, which passed between the odontoblasts, and where the dentinal fibril was pulled out from the dentine he could also trace them between these fibrils: from these observations he concluded that these nerve-fibres entered the tubes of the dentine. Boll was not successful in actually tracing them into the hard substance, but he appears to be the first observer who had succeeded in tracing them so far in their course from pulp to dentine.

Kölliker (1867), speaking of the nerves of the pulp, says: "As regards their endings, one sees, here and there, loop-like curves of the fibres, but it is beyond doubt that these are not the last endings."

Professor Klein [11], in 1883, says: "Numerous medullated nerve-fibres, forming plexuses, are met with in the pulp tissue; on the outer surface of the pulp they become non-medullated fibres, and probably ascend in the dentinal tubes."

Salter [25] was of opinion that there is a nerve supply to the dentine, both from the periodontal membrane and from the pulp, instancing cases in which a certain area of dentine remained sensitive after destruction of the pulp, and mentions that Czermak described a plentiful supply of nerves to this membrane, which he had traced to the hard tissues of the root of the teeth. I have myself seen very numerous nerve-fibres in the periodontal membrane in specimens impregnated with silver nitrate, but it is very difficult to procure sections in which they can be traced for any distance. Salter [26] concludes his discussion of the question by the statement that "the mode in which the hard tissues of the teeth are supplied with nerves is still an enigma, but that there *is* some supply is certain on physiological grounds."

I think we are all well convinced that dentine is a sensitive tissue, even although so great an authority as John Hunter considered that it is not. We may, I think, consider it an exquisitely sensitive tissue, and it has seemed very difficult to account for this great sensitiveness in the absence of any evidence of the actual distribution of nerves in its substance. Several histologists have attempted to account for sensation in the hard substance of the tooth apart from the actual presence

of nerves, considering that the soft material occupying the dentinal tubule conducted sensation to the nerves in the pulp. The principal supporters of this view have been Mr. Hopewell-Smith and Dr. Aitchison Robertson, although they differ in their views as to the actual anatomical path by which sensation is transmitted.

Mr. Hopewell-Smith [7] has long held the view that the function of the odontoblast cell is that of a nerve-end organ, sensation being conveyed through the dentinal fibril, which is a protoplasmic prolongation of this cell. He was able to show by means of teased-out preparations from the pulp that the nerve-fibres, when stained with methylene blue, took on the characteristic varicose appearance, and were seen in great abundance immediately around the odontoblasts. He has been unable to trace nerve-fibres into the cells, although they enclose them in a fine network. The great objection to this view—an objection acknowledged by Mr. Hopewell-Smith—is that the odontoblast cell with its process is not laid down in the embryo from the same layer of the blastoderm as the nerves. The nerves are epiblastic structures; the pulp cells are of mesoblastic origin; and it seems improbable that a mesoblastic tissue should form an important portion of the path of conduction of the impulses conveyed by an epiblastic tissue, although I am quite aware that tissues derived from the epiblast may be laid down in mesoblastic tissue, as instanced by enamels which are not wholly epiblastic, but, as Mr. Tomes says, “are laid down by the operation of epiblastic ameloblasts in a matrix which is derived from a modification of the surface of a mesoblastic dentine papilla.” Mr. Hopewell-Smith, in allowing the objection, says: “Accepting the statement of Schäfer (that all nerve-fibres and nerve-cells are originally derived from the neural or neuro-sensory epiblast) one is led to the conclusion that odontoblasts cannot possibly be, from the developmental point of view, ganglion cells in which sensory, or tactile, or trophic impulses arise *de novo*. But it is no argument against the idea that they serve as sensation transmitters.” In the absence of evidence of the passage of nerves into the dentine we can understand this to be a possible, although it has always seemed to me a rather improbable, explanation of the mode in which dentine transmits sensory impulses, but I do not think there has ever been any proof that such mode of transmission occurs in the mammalian tooth. The late Dr. Weil [34], of Munich, to whom we are indebted for the adaptation of the method of von Koch to the preparation of sections of teeth—a method which has proved of the greatest value—also held a similar

opinion, for he says: "As things stand at present nothing lies in the way of the theory that each delicate fibril of the basal layer of the membrana eboris is a means of connexion between the nervous system and the odontoblasts, and that the latter formations may be regarded as nerve-endings. By regarding the odontoblasts as capable of excitation, the sensibility of the dentine would be best explained." But he goes on to say that this is only an hypothesis that time may prove to be true, and must limit himself to saying that nerve-fibres or groups of such cannot be found beyond the cortical layer of the pulp.

Magitot [14] described certain ramified cells beneath the odontoblasts, which he said were in continuity by their processes with the nerve-fibres on one hand and the basal prolongations of the odontoblasts on the other, thus "forming a direct chain of sensation." The existence of such cells has, however, not been corroborated by other observers.

A somewhat similar view was upheld by Dr. Aitchison Robertson [21] in a paper contributed to the *Transactions of the Royal Society of Edinburgh* in 1891. From the examination of teased preparations in the dental pulp of the ox treated with anhydrochromate of potassium, he considered the pulp processes of the odontoblasts were in continuity with true nerve-fibres deeper in the pulp. He says: "I am convinced that the central processes of the odontoblasts become continuous with nerve-fibres." "Several demonstrations," he goes on to say, "were obtained showing that the pulp processes do pass into groups of nerve-fibres, amongst which they seem to run for some distance before they acquire a medullary sheath. The central process seems to become the axis cylinder of a nerve-fibre which gradually acquires a primitive sheath in which the medullary substance slowly accumulates till an ordinary medullated nerve results." He would thus look upon the odontoblasts and dentinal fibrils as the terminal organs of the nerve-fibres, and says: "We may regard the odontoblast and its peripheral process as an end organ, which, if not itself sensitive, at once transmits sensory impulses to the nerve with which it is connected." After a careful perusal of the paper and examination of the drawings, I cannot think the evidence of such a mode of nerve supply to the tooth is at all complete. One is aware that there is some analogy to this mode of termination in the endings of the olfactory nerves; from the olfactory cell, a nerve process proceeds towards the olfactory bulb, the peripheral process of the cell terminating in the olfactory hairs, but in this case the olfactory cell is an epiblastic cell, and the nerve-fibre represents apparently the axon of a true nerve-cell—

the cell and the nerve-fibre are formed from the same layer of the blastoderm. The gustatory cells in the taste-buds which were formerly considered to be in continuity with the nerve-fibres are, according to Schäfer [29], not in continuity with them. Dr. Carl Huber [9], of the University of Michigan (1898), by the use of methylene blue also traced nerve-fibres to the plexus beneath the odontoblasts and from that to what he considered their terminations at the inner border of the dentine. In this he corroborated the researches of Retzius [20], who in 1894 traced nerve-fibres in the pulp of the mouse to the inner surface of the dentine; but while Huber does not believe in the possibility of their entering the dentine, Retzius appears to be more doubtful on this point, for he says: "In vertical sections the fibres, like a string of tiny beads, stretch between the odontoblasts to the surface, and there end free. They often bend on reaching the surface, and run a little way tangentially. In a tangential section they can be partially traced under the dentine." One would imagine that the fibres he looked upon as under the dentine were really in the tubes.

In 1892 and 1895 Morgenstern [15] published his views on the distribution of the nerves to the hard tissues of the teeth. He made use of Golgi's method and described *medullated* fibres entering the dentine. He considered that they occupied tubes distinct from the dentinal tubules containing the dentinal fibril as well as running in these, and terminated either at the dentine-enamel margin or in the substance of the enamel, in the knob-shaped enlargements seen often in the crown of the tooth projecting into the enamel. He relied upon the methods of Golgi, and excellent as these are for many purposes, I do not think they are very applicable to the investigation of the nerves of the teeth; they often give rise to appearances which are very deceptive and lead to false interpretations, as I shall explain more in detail in treating of stains. I should be very unwilling to translate the thick black lines I have often obtained in the dentine in Golgi preparations as medullated nerve-fibres; they appear to me more in the nature of irregular deposits of the chromate of silver, but not having seen Morgenstern's preparations, I am unable to judge of the appearances which led him to the extraordinary conclusion that medullated nerves penetrated the dentine.

Professor Römer [22], of Strassburg, has been for several years engaged in an investigation of the nerves of the teeth. I think there can be little doubt that he succeeded in tracing nerve-fibres into the dentine, but he was unable to carry conviction with his specimens, which were, I believe, not sufficiently thin to enable him to procure

photographs, which are very difficult indeed to obtain, of this very delicate structure, even when the sections are sufficiently thin. He considered the nerves were most abundantly found at the cornua of the tooth and that the dentine of the root is entirely without nerves. On these latter points I am unable to agree with him, or that the normal termination of the nerves is to be found in the spindle-like enlargements which are seen at the enamel margin.

M. Pont [19] compared the odontoblasts to peripheral neurones (or nerve-cells with their processes) which occur in other peripheral organs, such as the retina, and considered that the nerve-fibres without forming any direct anatomical communication with the odontoblast, formed synapses, that is, that the nerves which envelop the cell transmit sensation from the cell to the afferent nerve, actual anatomical connexion not being necessary for the transmission of impulses from the peripheral cells. This, the neurone theory of Waldeyer [30], has been lately disputed, as it is maintained by some authorities that in these supposed cases of synapsis there really is a fine definite communication by neurofibrils across the supposed interval. The same objection would also hold good here, that we should not expect a synaptic any more than a direct communication between a cell formed from the mesoblastic layer and a true nerve-fibre of epiblastic origin.

In my paper before referred to I have described my own investigations on the nerve supply of the dentine, and I wish to avoid repetition as much as possible, but there are certain points connected with the subject which I may perhaps be permitted to discuss a little more in detail. It will perhaps be convenient to treat these points under separate headings, as this will enable me to emphasize more especially certain results which I have been able to obtain.

THE MEDULLATED NERVES.

These are very abundantly supplied to the tooth pulp and enter the tooth in company with the blood-vessels at the apical foramen. The main bundles of medullated fibres divide and subdivide in their course through the pulp, which is parallel with the long axis of the tooth, but still form quite large nerve-bundles at the periphery, where at a short distance behind the odontoblast layer they lose their medullary sheath and neurolemma, and the axis cylinder divides into very numerous neurofibrils which enter into a plexus immediately under the odontoblast cells. In fortunate preparations the expansion of the neurofibrils at the termination of the bundles of medullated fibres is beautifully shown.

THE PLEXUS OF RASCHKOW.

This is the first plexus of neurofibrils after their expansion from the axis cylinder and consists of an interlacement, and not an anastomosis of the fibres. In a paper read before this Section in March, 1908, by Mr. Law [12], he says, describing the fibres he observed in his sections: "The fibres are very much larger than one has been led to expect from earlier researches. Myriads of minute scopiform strands is the description by Röse, and other writers describe similar appearances of large numbers of interlacing fibres which have been called the plexus of Raschkow." Mr. Law says that in none of his sections has he been able to obtain such appearances, but has found the nerve-fibres to run almost in straight lines to the odontoblasts, and he ventures the opinion that "this so-called plexus is not composed of nerve-fibres at all, but is made up of connective tissue bundles running upwards and forming the structural skeleton of the pulp." I do not understand why Mr. Law did not see this plexus, which is brought out very clearly by a differential nerve stain which shows the beaded nature of its component fibres. My own experience certainly leads me to agree with Röse and others, that the neurofibrils are exceedingly minute. In young teeth especially, stained by Cajal's nitrate of silver method, an immense number of comparatively coarse connective tissue fibres traverse the pulp at right angles, or nearly so, to the surface of the dentine, but it can be seen, by daylight illumination especially, that these fibres are stained brown and the minute nerve-fibres are black.

I am afraid I cannot agree with Mr. Hopewell-Smith that his photograph on p. 119 of his work on "Dental Histology" represents the plexus of Raschkow; this plexus, as I have stated, consists entirely of fine non-medullated fibres, and no scraping from the inner surface of the dentine could possibly show this very delicate structure; such a preparation would show the larger medullated nerves mingled with blood-vessels and connective tissue fibres and not represent the plexus of Raschkow at all, in fact, it could not be separated by any teased-out preparation. From this plexus the nerve-fibres pass to the odontoblasts, in many cases enclosing them in a network of fibres, but the main trend of the fibres is more or less in straight or diagonal lines to the dentine.

THE MARGINAL PLEXUS.

The nerve-fibres have usually been described as terminating at the inner margin of the dentine, but my preparations show that on reaching this margin the fibres pass laterally and form a narrow continuous plexus along the surface of the dentine, from which fibres pass to the dentinal tubes. Instead of a terminal plexus we must then consider this to be more appropriately called the marginal plexus. It is well shown in fig. 1.

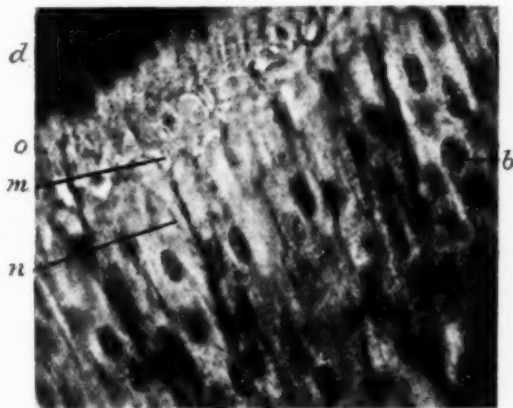


FIG. 1.

Photograph from a Weil (ground) preparation of a bicuspid tooth stained with Löwit's gold chloride, showing nerve-fibres (*n*) passing around the odontoblasts to the marginal plexus (*m*), and crossing the odontogenetic zone (*o*) to the hard dentine (*d*); (*b*) nuclei of odontoblasts. ($\times 800$.)

THE NERVE-FIBRES IN THE TUBES OF THE DENTINE.

In sections of young teeth the fibres can be seen to pass from the marginal plexus across the zone of partial calcification—the odontogenetic zone—occupying the tubules in that layer and again passing into the hard dentine as shown in fig. 2, which is from a Weil (ground) specimen stained by Löwit's gold chloride method. The nerve-fibres are very closely attached to the odontoblast cells and their processes. This is especially well seen where the fibrils have been pulled out from the dentine. Of course, it is almost impossible to obtain sections with

only one layer of dentinal tubes, and some confusion in the images is produced by the fibres in other tubes slightly out of focus, but in cases where single tubes have been more or less separated the nerve-fibres in the substance of the dentine can usually be seen in two rows of tiny beads, as described by Retzius, in the pulp. These beaded fibres can be traced all through the dentine, but become smaller and smaller as they approach the periphery; this is in accordance with the distribution of nerves which terminate in fine subdivisions in other parts of the body. As Mr. C. Tomes says [32]: "In those tissues which are naturally

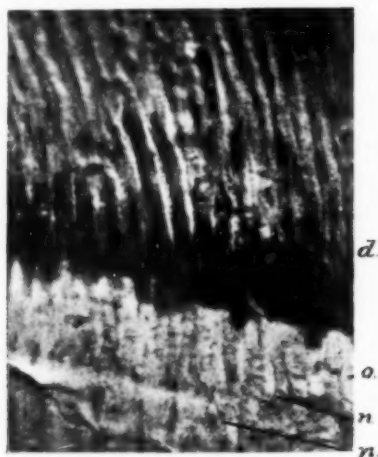


FIG. 2.

Photograph from a Weil (ground) preparation stained with Lowit's gold chloride, showing nerve-fibres (*n*) passing from the pulp across the odontogenic zone (*o*) to the hard dentine (*d*), where they are seen in the tubes.

so thin as to present great facilities for examination, nerves of a degree of fineness unknown elsewhere have been demonstrated; in other words, the easier the tissue is to investigate, the finer the nerves which have been seen in it, while dentine is among the most difficult substances conceivable for the demonstration of fine nerve-fibrils if such exist in it." The examination of a great many specimens, both ground and decalcified, has convinced me that these fine dotted lines in the final branches of the tubules beneath the cementum and enamel are in direct continuity with the larger beaded fibres seen at the inner margin of the

dentine where they enter the tubules. The dentine is everywhere penetrated by very fine lateral and diagonal branches of the main tubes, both in their course and terminations. I am aware that these branches have been usually described as very abundant in the roots and much less so in the crowns of the teeth. Mr. Hopewell-Smith [8] says: "They are less frequent or almost absent from the dentine of the crowns, where they are only found as the tube approaches its free



FIG. 3.

Drawing from a decalcified specimen stained with silver nitrate (pyridin method), showing the beaded fibres traversing the tubes just beneath the cementum. Human bicuspid. ($\times 600$.)

termination"; and Mr. Tomes [33] also says: "In the crown of a human tooth these fine branches are comparatively few until the tube has nearly reached the enamel."

It is difficult to obtain good penetration of the nitrate of silver at the enamel dentine margin so that the tubules appear at first to be

very little branched in this situation, but in cases where I have succeeded in staining an area of the dentine completely it is seen that the tubules are very abundantly branched and the fine divisions are filled with tiny black dots (fig. 3). The fine terminations beneath the cementum are more easily impregnated with the silver, but my specimens will show that when the dentine beneath the enamel has been persuaded to take the stain the branches are quite as abundant as they are elsewhere. It is on the borders of the fully stained portions that one sees with greatest distinctness the beaded nature of the tube contents—these little dots are seen to traverse the small branches to their most delicate terminations.

I feel quite convinced that the whole of the dentine is permeated with fine branches, their demonstration being merely a question of thorough penetration of the stain; wherever this has taken place innumerable interlacing branches are seen all across the dentine. The most successful demonstration of these branches is procured by the silver pyridin process, which I will describe when treating of methods of staining. Many tubes, as has been frequently described, terminate at the enamel margin in club-shaped and thick truncated endings, but mingled with these coarser tubes are very delicate tubules, finely dotted, and reaching the enamel. I would draw attention to the fact that the beading of the branches is quite as evident in calcified (Weil) preparations as it is in decalcified ones, showing that this appearance is not due to the action of the acid used in decalcification. In the slides on the screen, which are photographs of the pyridin silver preparations, the great length of some of the branches is very noticeable. The coloured drawings of these same preparations (drawn to scale with the Abbé drawing prism) will give a better idea of the appearances I have described than the lantern slide, in which the clear definition is confined to one plane. At the margin of the cementum the fibrils terminate in loops and very delicate, scarcely visible branches, many of which enter the granular layer and are finely beaded to their extremities. Under the enamel many of the tubules are much coarser, and some appear truncated, as often described, as if there had been an alternate process of absorption and deposition during the first stages of development of the tissues. Many tubes cross the borderline and terminate in various ways in the enamel, some by small, round, knob-like bodies, some by tiny flattened expansions, while others pass between the prisms in fine whip-like processes, but I have not been able thus far to trace the fine beaded fibres into the enamel.

In many teeth the so-called spindles are met with and the tubules communicate directly with them, but I have not been so fortunate as to secure a thorough impregnation with the silver in places in which these spindles are present. These bodies are very evident in some teeth, being often seen in great abundance surrounding the apices of the dentine cusps: here they seem to be arranged in a more or less regular manner, but others are seen isolated and often of very considerable length, and their connexion with the dentinal tubes admits of no doubt.

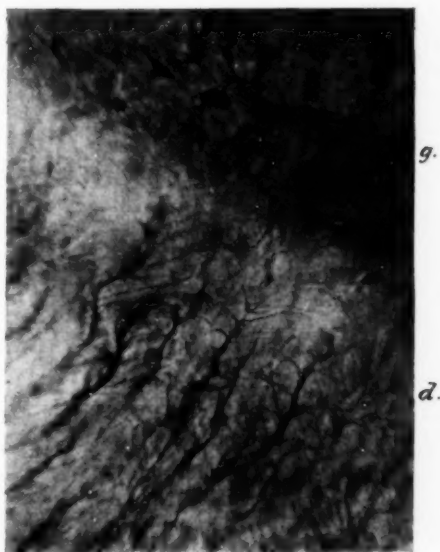


FIG. 4.

Photograph of a similar preparation to that illustrated in fig. 3. (*g*) granular layer of dentine; (*d*) dentine. Terminations of the fibrils at the cementum margin, showing the fine beaded terminal branches.

Various theories have been held as to the origin of these spindles. According to von Ebner [3] they pass between the prisms, and he considers that they are filled with air and are due to the shrivelling of the cement substance between the enamel prisms. Paul [18] looks upon them as the imperfect calcification of the first formed dentine, there being in the early stages of dentine development a thin band of transparent dentine matrix which has two sets of processes of formed

matrix, one communicating with the connective tissue of the pulp, which, together with von Ebner [4], I [16] have described as forming the scaffolding for the deposit of the lime salts of the dentine, and one extending between the ameloblasts, which are thus kept apart and form elongated spaces filled with imperfectly calcified matrix. Von Ebner and Wedl consider that there is an absorption of the first deposited dentine and that these persistent tubes and spindles have resisted absorption. Professor Römer [23] considers that these spindles contain organic matter which stains red with gold chloride, and looks upon them as containing a sensitive nerve-end apparatus. They would naturally draw attention in connexion with nerve-endings, as they so often show a central stem with little swellings and expansions upon it, giving it much the appearance of a special nerve-end corpuscle.

One of the slides which I show on the screen appears to show a very promising nerve-ending in its axis, but unfortunately for this interpretation the specimen is from a dry ground section of the tooth of an ancient Briton. There is some danger that if this had been found in a fresh tooth it would have been looked upon as a nerve-end corpuscle. I am not, however, at all prepared to say that nerve-endings may not be found in these spindles. I think it is extremely likely that they may, but I do not think this would prove any normal innervation of the enamel. In this connexion I may quote some very interesting remarks by Mr. James Salter in his work before referred to, published in 1874 [27]. He says: "Enamel and dentine are both liable to defects of original structure. The enamel rests on the surface of the dentine and between its fibres, the dentinal tubes project more or less. A continuation of the tubes by small contracting narrow points is a natural condition, but occasionally these prolongations assume the form of elongated bulbous cells, still clearly connected with the ends of dentinal tubes. They often exist to an extent that is clearly abnormal, large, long, branched excavations passing a considerable way towards the exterior of thick enamel. I have shown that these cavities are really prolongations of the dentinal tubes and that they have the same definite walls as the tubes themselves. Presuming that the dentinal tubes are in some way the main vehicles of tooth structure sensibility, this condition would endow the enamel with an abnormal perception of external agencies, and this probably explains some of those cases of hyper-sensitive teeth which occur in persons of early age, where the enamel has not yet been sufficiently worn to reach the dentine."

I may perhaps say in this place that an extended examination of

Weil preparations has convinced me that the enamel is penetrated to a very considerable extent, although irregularly, with dentinal tubes and probably portions of the dentine matrix, and I am disposed to agree with Mr. Caush that despite the results of chemical analysis the enamel does contain spaces capable of taking a stain and would not be so entirely out of the pale of nutrition as we have been led to suppose. Dr. Fischer [6], in his interesting lectures on dental histology, is of the same opinion. It may be that these spaces into which stains penetrate are so small that they would not affect a chemical analysis, but we must remember we are dealing with microscopical details.

A very curious appearance in the dentine was described by Dr. Dentz, of Utrecht, many years ago (in the year 1892), which he was inclined to look upon as a nerve-end organ. The specimens were from a developing tooth in which about half the dentine was formed, and show a row of pear-shaped bodies with large nuclei. They are, however, much too large ($\frac{1}{400}$ in.) to be interpreted as any normal nerve-endings in the dentine, and I have only heard of one other specimen in which similar bodies were found. They have been generally considered to be pathological, due to some defect in development.

THE BASAL LAYER OF WEIL.

The so-called basal layer described by Weil is a clear space in the pulp immediately beneath the odontoblasts, often very evident in sections ground by the balsam process and sometimes also seen in sections of decalcified teeth. In a paper which I contributed to this subject in 1892 I pointed out that the existence in this layer of blood-vessels which showed perfectly rounded contours was an argument against its being due to a stretching of the tissues in the process of preparing the sections as suggested by von Ebner and Röse. I did not also agree with Dr. Weil that the delicate fibres visible in this layer were all in communication with the basal ends of the odontoblasts. Many of the larger fibres are, but the finer fibres pass between and around them to the dentine, becoming incorporated with its matrix. With respect to Dr. Weil's statement that blood-vessels are not found in this layer, we know that this was an error of observation—they are frequently seen in this situation. Mr. Hopewell-Smith shows a photograph on p. 146 of his book in which a blood-vessel is well seen in the basal layer in a decalcified tooth, and I have many Weil specimens also showing them.

Noticing that balsam preparations fully stained with iron and

tannin did not show the layer of Weil, I thought it most probable that this space was occupied chiefly by nerve-fibres which were not stained by ordinary methods, and concluded that if I could re-stain a specimen which showed this layer distinctly, with a nerve stain, I might be able to prove this point. I therefore removed the balsam from a very clear and thin specimen, showing the layer, by immersing it for some time in chloroform; I then passed it through alcohol to water and re-stained it with chloride of gold by Beckwith's method, in which no acid is employed. The result of this experiment I show upon the screen. The first photograph was taken from the section in its original condition, stained with borax carmine: it shows the space beneath the odontoblasts very clearly, and also shows that the partially calcified dentine layer on the farther side of the odontoblasts is clear and unstained. In the second photograph it will be noticed that the layer of Weil is not visible any longer as a clear space, and that the odontogenetic zone is now dark and filled with fine fibrils, which under a high power are seen to be nerve-fibres passing into the dentine. I hope these photographs will make it evident that the layer of Weil is not a basal layer, that it is not produced by stretching of the tissues, but is a part of the pulp occupied by connective tissue fibres, and by a dense plexus of fine nerve-fibres. In the photographs of decalcified specimens which I have already shown on the screen it is also seen that this space is occupied by a dense mass of nerve-fibres and connective tissue. It is at the inner margin of this layer that the bundles of medullated nerve-fibres spread out into the smaller branches and pass parallel to the surface of the dentine, and it is here that they lose their medullary sheath and break up into a plexus of very delicate neurofibrils, which before passing to their distribution in the dentine occupy this area.

STAINING.

I will refer only very briefly to the methods I have employed in this investigation. The earlier methods I used I only look upon as leading up to those I now make use of. Of these the principal ones are Cajal's silver nitrate impregnation (for very young teeth) and a method in which the reduction of the silver is facilitated by the employment of pyridin. This is an adaptation of one of those used by Levaditi to demonstrate the *Treponema pallidum* in the tissues. It is very similar to the method of Cajal, but the reduction of the silver is facilitated by the addition of pyridin and acetone used in combination with the pyrogalllic acid or

hydroquinone reducer. The chief objection to this method is the exceedingly penetrating and unpleasant odour of the pyridin. Some of my best specimens have been obtained by the use of this combination. It can be used with specimens in bulk before decalcification or as a preliminary to the Weil process and combined with a nuclear stain such as borax carmine. For gold impregnations I have made use of Ranvier's modification of Löwit's formic acid process, and for calcified sections



FIG. 5.

Drawing from a decalcified specimen stained by the silver nitrate and pyridin method. (p) pulp in which is seen a small bundle of fine neurofibrils extending to the plexus of Raschkow (r), passing between the odontoblasts to the narrow marginal plexus (m), and passing along the tubes in the odontogenetic zone (s), to the hard dentine (d); (b) blood-vessels. ($\times 600$.)

in Weil specimens of Beckwith's modification of Freud's process as recommended by Dr. Sims-Woodhead [31]. The great advantage of this is that no acid is employed, which makes it especially applicable

to Weil sections. The sections are first immersed in chloride of gold (1 per cent. solution) for three to four hours, then washed and treated for three minutes with a 20 per cent. solution of caustic soda, again washed and immersed for half an hour in 10 per cent. carbonate of potash, which is drained off and the gold finally reduced with iodide of potassium 10 per cent. for about fifteen minutes. This method gives a very distinct stain free from deposits, but my specimens are too recently prepared for me to form any opinion as to the permanency of the stain. Golgi's method I have tried and am still treating teeth by this process, but so far have not met with much success. Although one would not think of disparaging a method by which so much excellent work has

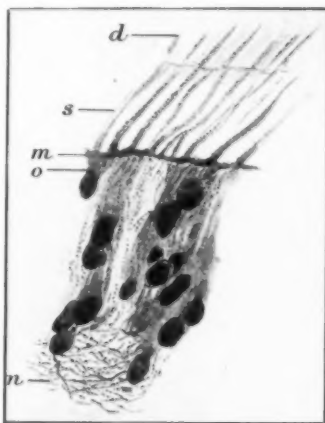


FIG. 6.

From a decalcified specimen stained with borax carmine and silver nitrate (pyridin). (n) the nerve-fibres in the plexus of Raschkow; (o) odontoblasts; (m) marginal plexus; (s) odontogenetic zone; (d) completed dentine. ($\times 600$.)

been done and which has revealed so much in the minute anatomy of nerve tissue, I do not think it is one which is very applicable to the investigation of the nerves of the teeth. The impregnation is only partial, but the portions stained are stained very intensely and enable fibres to be traced through a great part of their course, but it stains other tissues as well as nerves and frequently gives precipitation forms of chromate of silver. These objections make it very necessary to use great care in interpreting appearances procured by the method, although

for the reasons I have stated it is very valuable as a corroborative method to interpret appearances in other preparations. Bolles Lee [13] mentions in his "Microtomist's Vade Mecum" that a correspondent informed him he had Golgified a potato and obtained beautiful nerve-fibres. I may say here that although fairly thick sections of Golgi preparations may be desirable in tracing nerves in other tissues they are absolutely useless in teeth—the sections must be thin to be of any value at all. Any section treated with silver nitrate will generally show portions completely blackened, but a successfully stained portion, at all events by the pyridin method, will show the dentinal fibril stained brown and the minute beaded fibres as a succession of black dots in the brown stained tubule.

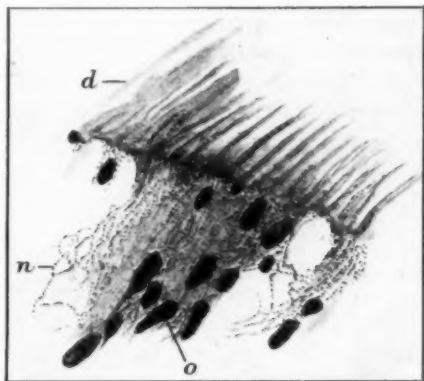


FIG. 7.

From a decalcified specimen stained with borax carmine and silver nitrate (pyridin). (d) dentine; (o) odontoblasts; (n) nerve-fibres. In several places where the pulp has become a little separated from the dentine the detached nerve-fibres are well shown. ($\times 600$.)

At the suggestion of Dr. Spriggs I have for some time past abandoned the use of nitric acid for decalcifying purposes, and now employ formic acid exclusively in a 33 per cent. solution. The formula as given by Professor Fischer [5] is: Formic acid, 33.3; distilled water, 76.7; formalin (40 per cent.), 5. If the tissues have been hardened in formalin the formic acid can be used without it. In specimens treated in this way the odontoblasts appear to be very little or not at all shrunken, as they certainly are often to a great extent when mineral

acids are employed. Many histologists have, especially of late, discarded the use of alcohol in preparing sections of soft tissues, as this always causes more or less shrinking. I have spoilt many a good specimen in the course of dehydration and clearing, and now prefer to cut all sections in the freezing microtome and mount them in watery solutions—either Farrant's solution or glycerine. Of course, in the preparation of Weil sections alcohol must be used, but the very gradual increase of the strength of the alcohol in this process where the tissues are treated in bulk reduces the risk of shrinkage to a minimum.

It has been suggested that I should deal with the physiological and anatomical bearings of the result of this investigation, but it has been a purely histological one and I have carefully avoided any theories. The point seems to be this: Do the nerves pass into the dentinal tubes and traverse the dentine or do they not? I have endeavoured to show that they most certainly do, and if this anatomical fact is considered proved the explanation of certain apparent anomalies in the sensibility of the dentine will have to be carried out in accordance with this fact.

It does not appear to me that the phenomena of pain in the teeth are so very mysterious. It seems to fully accord with the fact of the existence of nerves in the dentine that we should in the first stage of caries have more pain than in the later stages. We are here dealing with the fine divisions of the nerves at their final distribution. It is a well-known physiological fact that pain is referred especially to nerve-terminations; instancing one example only, the pain in the knee in hip disease, and in the earliest stages of caries the destruction of the delicate nerve tissue by the acids of decay which probably takes place later, has not occurred to any appreciable extent. Hence, it does not seem any anomaly that the sensibility of the tooth decreases as caries advances, until the pulp is approached, with its high vitality and blood supply, where the mass of nerve tissue will still be in functional activity. We cannot disprove the anatomical facts by any phenomena which are difficult to reconcile with them; all we can do is to seek for some explanation which shall bring these phenomena into line with the ascertained facts.

SUMMARY.

To sum up the conclusions to which these investigations have led me: The nerves of the dental pulp lose their medullary sheath and neurolemma just beneath the odontoblast layer, and are seen to form an intricate plexus of neurofibrils in this situation, the plexus of Raschkow; from this plexus they pass in approximately straight lines between and around the odontoblast cells and form another much narrower plexus at the inner margin of the dentine, which I have called the "marginal plexus." They very closely envelop the cells and the dentinal fibril, and enter the dentine in company with the latter. They can be traced as fine beaded fibrils all along the tubes and their very numerous branches, and are seen to terminate in the fine ramifications of the dentinal tubes beneath the enamel and cementum. Whether they actually pass into the enamel in places where the tubes penetrate this tissue I am unable at present to say, but consider that in any case their normal and principal final distribution is within the limits of the dentine. They are apparently very evenly distributed around the larger portion of the pulp, becoming scattered, although not entirely absent, as they approach the apex of the root.

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DISCUSSION.

The PRESIDENT (Mr. H. Lloyd Williams) expressed his great appreciation of Mr. Mummery's very beautiful work. To him, at any rate, the conclusion seemed to be most convincing.

Mr. F. J. BENNETT thought Mr. Mummery might summarize his work in the memorable words of Lord Beaconsfield when he said, "I have begun many things often and I have usually succeeded at last." That Mr. Mummery had succeeded he thought very few would call in question. A great many speculations had been put forward as to the various tissues, and it seemed as though we should have to learn again the meaning of such terms as Tomes's fibril, odontoblasts, and other structures, and to ask anew what were their functions. A point Mr. Mummery seemed to take for granted was that these nerves were for the purpose of sensation, and that might be the case, but it was a cause for wonder as to why teeth should be considered organs of such acute sensation. There were certainly many tissues, not so highly supplied with nerves, which responded more quickly. Another view might be put forward—namely, that the nerves were concerned in the intimate repair of the tissue which in the normal man was subject to wear and tear. There was a peculiarity in the way in which repair took place, due to the manner in which the dentine was laid down. As was well known, the dentine of repair was not laid down exactly in the corresponding place where the wear and tear took place—i.e., it was not at the shortest distance.

from the pulp to the point of injury, re-formed dentine taking a sinuous or oblique direction in many cases. It seemed to him that if it were merely a question of sensation being conducted through the tooth the dentine of repair would be found deposited at the nearest point, whereas it was at a point more distant and corresponding to the exact method in which it was laid down. He thought it was possible the nerves might have something to do with the way in which repair took place in the manner he had described. There was still a good deal of ignorance as to the enormous distribution of nerves in the pulp, and the fact that the dentine should be practically a mass of nerve-fibrillæ was almost incomprehensible. It was difficult to understand in a structure which was not obviously a very sensitive one or one that underwent rapid changes. If it were the kidneys or liver, in which constant and frequent changes were going on, one could understand the nerve supply, but in the case of the teeth it was difficult to understand. The Section was glad to have such facts as Mr. Mummery had brought forward that evening. The perfection of his specimens was the despair of the ordinary histologist and they were things to be highly prized.

Mr. GABELL said that having been one of those privileged to see the actual specimens at leisure, and having carefully examined them, he could say it was wonderful workmanship and he had never seen anything so beautifully done. The difficulty of preparing the sections was immense, and Mr. Mummery had overcome it to a remarkable degree. In the specimens under the microscope, with the finger on the fine adjustment, the distribution of nerves was rendered very evident, as Mr. Mummery had shown in his drawing. For the inexperienced microscopist perhaps the earlier photographs were not so convincing, but the drawings were an exact reproduction of what the slides actually showed. The Section had to thank Mr. Mummery for a most laborious task wonderfully well carried out.

Mr. STANLEY MUMMERY said he had had the unique opportunity of watching the investigation from the beginning, from the very first slides that suggested the possibility of nerves running through the dentinal tubes. As staining methods were improved the slides became more suggestive, until at last such slides were produced as those that had been shown that evening. He believed that anyone who had examined them as he had done could not help being convinced of the truth of the results. He could also testify to the enormous amount of time and labour that had been devoted to the preparation of the slides and specimens.

Mr. H. BALDWIN wished to pay his tribute of thanks to Mr. Mummery for his magnificent piece of work. There did not seem the slightest possibility of doubt that the explanations given were correct, and the clinical aspect of the case was fully corroborated by the investigations. Everyone was aware, no doubt, that dentine was a sensitive structure, and he thought most dentists had been simply waiting for some great microscopist like Mr. Mummery to prove

its innervation; and it was very satisfactory to him to be able to be present that evening to hear so epoch-making a paper read.

Mr. J. HOWARD MUMMERY, in reply, said that if the odontoblasts were engaged in active secretion they must have a certain nerve supply, and that many of these nerves might have a trophic function, but how such supply was conducted to them was a point that had to be settled by future investigations. He did not think there were too many nerves to supply the teeth. There were a great many in the pulp, of course, but when it was remembered what a large number of tubes there were in the dentine and the way in which they were spread out, this multiplicity could be accounted for. He agreed with Mr. Gabell that the photographs were not nearly so convincing as the specimens themselves, but photographs were exceedingly difficult to obtain. He thought, however, the last photograph he had shown *was* convincing and better than any drawing, the photograph having brought out the nerves in places where the eye could scarcely see them at all. To prove the case that the nerves of the pulp penetrated the dentine it was only necessary to see one tube with a nerve-fibril running along it, and he had shown the fibrils entering into six or seven tubes; in fact, all the tubes within that field of the microscope.

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OF THE
ROYAL SOCIETY OF MEDICINE

VOLUME THE FIFTH

COMPRISING THE REPORT OF THE PROCEEDINGS FOR THE
SESSION 1911-12

OTOLOGICAL SECTION



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1912

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The Council think it right to state that the Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Otological Section.

October 20, 1911.

Dr. W. MILLIGAN, President of the Section, in the Chair.

PRESIDENTIAL ADDRESS.

Modern Developments in Aural Surgery and the Present Position of Otology in the Medical Curriculum.

SINCE the Otological Society of the United Kingdom was founded in 1900 many important changes have taken place, not the least being its absorption by and its establishment as a separate Section of the Royal Society of Medicine. The original membership of the Otological Society of the United Kingdom was 57; to-day the Otological Section of the Royal Society of Medicine numbers 156. This large increase in membership, combined with recent developments in otological work, and a general expansion of its literature, has influenced your Council in deciding to hold six meetings in London instead of four, as formerly, and an extra-Metropolitan meeting as well, when such can be conveniently arranged.

Much of the recent progress in otology, both in this country and abroad, has been due to advances in bacteriology, to more accurate pathological research, and to improvements in surgical technique. Another factor, which to my mind at any rate has done much to mark progress and to elevate the position of otology in the medical landscape, has been the more intelligent and generous provision by hospital boards, both lay and medical, of facilities for the adequate treatment of persons suffering from diseases of the organs of hearing. The day has passed when the aural clinic is relegated to the tender mercies of the most

recently appointed member of the surgical staff, a gentleman whose interests in all probability ran in quite different grooves, and whose absence from the clinic was more frequent than his presence. Nor, again, are unintelligent and mischievous regulations, such as that the aural surgeon must confine his attentions to out-patients and to the outside of the skull-cap, framed by intelligent medical boards of the present day. Encouragement, rather than discouragement, is now meted out to the Chef de Clinique, and opportunities are afforded to him to persevere in his endeavours to add some quatum to the sum of human knowledge of diseases of the ear.

To a large extent this gradual evolution of our speciality, slow as it has been in this country, has been forced on by the unalterable law of demand and supply. The public have clamoured for a more rational and scientific treatment of diseases of the ear, and the more enlightened hospital boards throughout the country have grasped the situation and have appointed specially qualified officers to take charge of special aural clinics. But if the position of the aural clinic and of its appointed officer is more satisfactory, is it so also with the position of the medical student?

To-day more than ever do we require efficient and properly trained aurists to deal with the vast numbers of school children who are being examined under the Medical Examination of School Children Act. Have the majority of the medical inspectors the necessary qualifications to adequately and thoroughly discharge this onerous duty—a duty to the individual as well as a duty to the State? Have our universities and teaching schools foreseen what was coming, and if they have, what have they done to assist in the matter? The most generous critic of our university system must, I fear, admit that *adequate* legislation relative to the teaching of otology has been practically *nil*, and also that hundreds of graduates are turned out year after year by the medical mill with a most rudimentary knowledge, if knowledge at all, of the principles and practice of aural surgery.

When President of the Otological Section of the British Medical Association in 1902 I ventured to try to stir up enthusiasm in this matter by suggesting that in the interests of patients suffering from exanthematous diseases, one of the most prolific sources of ear disease, applicants for resident posts in fever hospitals should be required to produce evidence of their having attended a course upon diseases of the ear and of their having some practical acquaintance with the subject. On another occasion, in order to endeavour to encourage interest in

otology and to make sure that the young specialist's knowledge was the result of genuine work, both practical and theoretical, and not merely the outcome of a few months' visit to the chief Continental clinics, I suggested that the various British universities should so arrange matters as to allow any candidate who so desired it to proceed to an honours degree in otology, evidence being forthcoming of his having had both theoretical and practical instruction over a given period.

Both suggestions fell upon academic ears too deaf to receive any mental impression, and so far we are to-day practically as we were ten years ago. But a time has come when it appears to me that we, as a Society of British otologists should be up and doing, and should make representations to the universities and teaching bodies throughout the country that in our opinion the attendance of the medical student for from three to six months at a recognized aural clinic should be made *compulsory*.

So far as I have been able to ascertain not one of the universities of the United Kingdom insists upon its students having a practical and theoretical acquaintance with otology prior to qualification, while the only London Medical School which insists upon its students attending its aural clinic is the London Hospital.

A step such as this, i.e., making otology a compulsory subject in the curriculum—the thin end of the wedge, no doubt—would within a few years be productive of much good and would ensure for the public a more rational and intelligent treatment of diseases of the ear than exists at present in many parts of the country. Doubtless any such proposal would be met with opposition, but it appears to me that if this Society is to justify its existence, its influence and energies should be directed to endeavour to secure the greatest good for the greatest number; that besides being a Society for the education of its existing members it should be National in its aspirations, and should so influence medical politics as to ensure that the medical student and practitioner of the future shall possess a more extended and practical acquaintance with diseases of the ear than he has had in the past.

Such a consummation is heartily to be desired and would, if accomplished, of itself amply justify the existence of this Section of the Royal Society of Medicine.

Three Cases of Chronic Suppurative Otitis Media.

By W. MILLIGAN, M.D.

**CASE I.—LOCALIZED EROSION OF EXTERNAL SEMICIRCULAR CANAL;
OPERATION; RECOVERY.**

J. K., MALE, aged 25, was admitted to hospital on March 15, 1911, on account of chronic left-sided suppurative middle-ear disease and frequent attacks of vertigo. Right ear: Operated upon three years previously for mastoid disease and sinus thrombosis. Left ear: Large perforation, foetid discharge. Cochlea: Ordinary conversation fairly well heard; high and low tuning forks lateralized to left ear. Right internal ear: Functionless. Vestibulo-canalicular system: No spontaneous nystagmus, but "fistel-symptom" well marked even on pressing tragus inwards. Caloric tests: Right, no reaction; left, 40 seconds: Rombergism, +.

Operation: Mastoid opened; cholesteatoma present; large fistula in external canal. Toilet of affected area.

After operation: Good progress; slight improvement in hearing; pulse remained very slow (48—60) for a week, and then became normal. Discharged April 7, 1911.

September 18, 1911: Ear dry and completely healed; no vertigo; hearing slightly better than before operation.

**CASE II.—LARGE EROSION OF EXTERNAL SEMICIRCULAR CANAL;
OPERATION; RECOVERY.**

A. L., MALE, aged 35, was admitted to hospital on April 25, 1911, with history of suppuration from right ear of ten years' duration; recently occasional attacks of severe vertigo. Temperature, 98.2° F.; pulse, 74; respirations, 16 to 18.

Right ear: Large perforation of membrane, scanty foetid discharge; no mastoid tenderness. Cochlea: Hearing power, $\frac{1}{80}$: tuning forks lateralized to right ear. Vestibulo-canalicular system: Spontaneous nystagmus, quick movement directed away from lesion. Caloric reactions: Nystagmus increased with either hot or cold syringing, most marked with cold; induction period, 45 seconds. Well-marked "fistel-symptom," but not produced on pressure over tragus. Rombergism marked—with eyes shut and feet together, falls to right side.

Operation: Antrum opened; bone sclerosed; cholesteatoma found; large fistula in external canal. Toilet of part. Patient discharged May 22, 1911.

August 24: Ear quite dry, no vertigo or other discomfort.

CASE III.—EROSION OF EXTERNAL SEMICIRCULAR CANAL;
LABYRINTHITIS (?).

J. F., MALE, aged 17, was admitted to hospital on September 15, 1911. Left-sided suppurative middle-ear disease of fifteen years' duration. Three weeks before admission began to have frequent attacks of vertigo accompanied by vomiting, quite irrespective of the ingestion of food. Temperature, 99.8° F.; pulse, 80; respirations, 18. Ear: Left meatus entirely blocked with granulation tissue; foetid discharge; slight mastoid tenderness, but no oedema. Cochlea: Watch not heard, loud conversation just heard. Low-toned tuning forks just heard in left ear, but referred to right side; high-toned forks referred to and heard in right ear. Vestibulo-canalicular system: Spontaneous nystagmus present, quick movement directed away from lesion; no "fistel-nystagmus." Caloric reactions: No definite reaction with either hot or cold water (nullified by presence of granulation tissue?). Gait: Patient steady on his feet when walking or when standing with feet together and eyes closed. On attempting to stand with eyes closed and upon one leg, falls over to left (affected) side. Knee-jerks markedly increased; no ankle-clonus; no Babinski or Kernig's sign. Urine normal.

Operation: Complete post-aural operation performed. Large fistula in external canal surrounded by an area of apparently necrosed bone. No pus seen to exude. Discoloured bone removed with fine burr, but membranous canal not opened. General toilet of infected area.

Progress since operation good, although nystagmus more marked. Should expectant treatment be continued, or should the labyrinth be extirpated?

DISCUSSION.

Mr. A. CHEATLE asked where the erosion was in each of the cases, if the President could localize it.

Dr. DAN MCKENZIE remarked that Dr. Alexander had drawn attention to this particular class of case in several articles which he had recently published.¹ He regarded the first three cases as obvious instances of localized labyrinthitis,

¹ *Archiv f. Ohrenheilkunde*, Leipz., 1910, lxxxii, pp. 1-21.

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which had been cured by the radical mastoid operation. The mastoid operation could be depended upon in most cases to cure labyrinth disease of this type. The third case of this series was one which occupied a more doubtful position. In such cases Alexander relied upon the subsequent conditions for guidance as to whether a labyrinth should be opened, and the symptoms upon which he laid most stress were the continuance of the vertigo, the presence of pain, discharge, and headache, particularly occipital headache. If such symptoms were present it was not wise to wait, lest the disease should extend beyond the boundaries which Nature had already set up.

Mr. RICHARD LAKE remarked that if there was only nystagmus and no giddiness or vertigo he could not see that there was any object in proceeding further.

Dr. DUNDAS GRANT said he had under his care a case in which there was very marked nystagmus, with distinct labyrinthine disturbance, before the operation, and after the operation, as in the President's case, the nystagmus was, if anything, more marked for a time than before. That was not altogether unexpected. The patient was kept in bed, and the nystagmus diminished to some degree. At present it had almost disappeared, the patient had no giddiness, and was infinitely better than before the operation, in spite of the fact that the subsequent course of the radical operation as such was not all that could have been wished; that is, the patient was withdrawn from his care, and a considerable amount of narrowing took place in the passage, amounting to almost complete occlusion. Not much time had elapsed since the operation in the President's case, and he did not think that the nystagmus rendered it necessary, in the absence of other symptoms, to do a further operation.

Mr. H. E. JONES said he agreed with the view just expressed by Dr. Dundas Grant. He had seen three or four cases of the kind in which, without further operation, good recovery ultimately took place, with good function.

Mr. SYDNEY SCOTT had taken some interest in the subject under discussion. Speaking from the operative point of view, in the first two cases he would have done as the President had done. As to the third case, he would like to know the meaning of the term "apparently necrosed bone." If at the time of the first operation necrosed bone was found, and also absence of vestibular reactions in the labyrinth had been noted, he would have proceeded further and operated on the labyrinth straight away. If in the present state of the patient there were persistent granulations, he would still operate on the labyrinth. Otherwise, if the cavity is healed and dry, in spite of the nystagmus he would not now touch the labyrinth.

The PRESIDENT (Dr. W. Milligan), in reply, said his wish had been to elicit from any member a hint as to whether one ought to simply watch and follow out expectant treatment in Case III, or whether something more ought to be done. In reply to Mr. Cheate's question, the erosion in all the three cases was on the external canal and towards the posterior limb of that canal.

With regard to the remarks upon Case III, he felt much indebted to those who had spoken. His own feeling had been to leave the patient alone, and he had not done anything further up to the present. The patient had no headache or sickness, but he had unquestionably developed more nystagmus since the operation. As, however, his general condition did not seem to be getting worse, he had left him alone. In answer to Mr. Scott as to the meaning of the term "apparently necrosed," the condition of the bone when the radical mastoid operation was performed was that the bone round the fistula was discoloured, being almost black. The appearance of the wound was now quite good. There were no granulations, and, taking into consideration what Mr. Scott, Mr. Lake, and Dr. Grant had said, he proposed to continue expectant treatment.

Temporo-sphenoidal Abscess following Chronic Suppurative Otitis Media ; Operation ; Recovery.

By W. MILLIGAN, M.D.

PATIENT, male, aged 28. History of prolonged suppuration from right middle ear ; severe headache of a few days' duration. Right membrane perforated, posterior superior segment ; foetid discharge. Tenderness over antrum, but not over temporo-sphenoidal or cerebellar area. Pulse, 90 ; temperature, 102° F. ; respirations, 16. Eye : Suspicion of ptosis upon right side ; no nystagmus ; no neuritis. Reflexes : Knee-jerks active, ankle-clonus present ; Babinski upon left side. Urine normal. Cerebro-spinal fluid cloudy, albumin slightly increased ; polymorphonuclears increased ; no organisms. After admission, temperature gradually dropped to normal ; pulse became very slow (44) and respirations 14 ; rapidly increasing mental hebetude.

Operation : Antrum opened ; cholesteatoma found. Base of temporo-sphenoidal lobe exposed ; dura covered with granulations. Incision into temporo-sphenoidal lobe ; abscess found and about 2 oz. of pus evacuated. Abscess drained by insertion of one tube through roof of antrum and another through the squama. Pus in abscess showed Gram diplococci.

Discharged five weeks after operation.

DISCUSSION.

Mr. WAGGETT desired to ask a question in regard to technique—i.e., as to drainage. Many surgeons, perhaps, did not get a sufficient number of those cases to form a habit ; a case every two months or so was not enough. He had just operated upon a case in which there was a very large

temporo-sphenoidal abscess containing 3 oz. of pus. At the instigation of a colleague he removed the drainage-tube at the end of two days, there being no further discharge. Up to the present, some fourteen days after operation, the result had been excellent.

Mr. C. A. BALLANCE said that for an abscess in any part of the body containing 2 oz. or 3 oz. of pus, he thought it would be wise to leave the drainage-tube in a longer time. In brain abscess he generally used a couple of drainage-tubes, removing one in five days, and taking out the other a little later. Much depended on the nature of the particular case, and he did not so much take the tubes out as let them come out of themselves. As the liquid brain tissue closed round the cavity the tube came out. He had had to reintroduce a tube on several occasions, and for that reason he was very careful not to take tubes out too early.

Mr. HERBERT TILLEY wished to ask whether the question of the retention of the tube did not largely depend on whether the abscess was acute or chronic. If chronic, the tube must be left in much longer, because the capsule was not elastic. In an acute abscess, even at the time of operating, the tube was liable to be pressed out by the contraction of the surrounding brain substance, and hence the tube could be removed more quickly than from a chronic case, in which one had to allow for the contraction of the capsule.

Dr. URBAN PRITCHARD said the procedure as to drainage depended also on the depth of the abscess. He was reminded of a case in which there were two abscesses. One was opened, and the other could not be found until some days afterwards, when it was opened into by a pair of forceps. A drainage-tube had to be inserted deeply, and it would not have done to have removed the tube in two days. This case occurred fifteen years ago, and the patient was now absolutely well.

Mr. A. L. WHITEHEAD thought one could scarcely keep a tube in too long in chronic cases. In acute cases drainage for a shorter time sufficed. In large abscesses he put in two tubes, side by side, and kept one tube in situ as long as there was any discharge of breaking down brain substance. In chronic cases it was his custom to wait for the tube to be pushed out by granulation tissue.

The PRESIDENT replied that one tube in this case was through the roof of the antrum, and the other through the squamous portion of the temporal bone, so that there was established through drainage. Much had been said about the desirability of allowing the tube to be extruded by granulation tissue forming behind it. He had never felt justified in removing a tube so early as on the second day, but, as Mr. Tilley said, much depended on whether the abscess was acute or chronic. It was his practice to drain chronic abscesses by means of tubes, and acute abscesses with gauze. The Council of the Section had arranged for a discussion on intracranial suppuration, and the discussion would include the very important question of the drainage of brain abscesses.

**Temporo-sphenoidal Abscess following Chronic Suppurative
Otitis Media ; Operation ; Death.**

By W. MILLIGAN, M.D.

PATIENT, male, aged 21, admitted to hospital in semi-unconscious state ; roused with great difficulty ; unable to answer questions. Left meatus full of pus ; perforation of posterior segment of membrane ; no granulations ; definite pain over antrum. Temperature, 99.4° F. ; pulse, 58 ; respirations, 18. Head slightly retracted, obvious pain on moving it. Eye : No neuritis, ptosis, or nystagmus ; slight convergent squint. Reflexes : Knee-jerks increased ; no ankle-clonus, no Kernig's sign ; right Babinski. Cerebrospinal fluid, under pressure, milky in appearance ; increase of polymorphonuclears ; no bacteria. Albumin 0.16 per cent.

Diagnosis : Intracranial abscess (temporo-sphenoidal or cerebellar ?) with meningitis. Complete post-aural operation. Temporo-sphenoidal lobe opened ; abscess found and drained ; pus in abscess contained large numbers of Gram diplococci (*Diplococcus catarrhalis*) ; no streptococci or staphylococci.

After operation : No marked improvement ; pulse irregular, between 48 and 60 ; temperature, 99° to 100° F. ; mental condition bad. Another lumbar puncture performed ; fluid much as before, slightly more coloured ; no bacteria. Cerebellum explored through posterior antral wall ; no pus found. As signs of meningitis increased, repeated lumbar punctures were performed every thirty-six hours, and amount of albumin estimated. First puncture, 0.16 per cent ; second puncture, 0.16 per cent. ; third puncture, 0.17 per cent. ; fourth puncture, 0.18 per cent. ; fifth puncture, 0.2 per cent. Urotropine given internally. Condition of patient worse. Temperature higher ; pulse varying from 48 to 72. A week later, patient improved greatly, able to move head without pain ; retraction passed off ; mental condition also improved. Ten days later marked relapse ; spinal puncture, however, showed marked improvement in cerebrospinal fluid ; clear, no organisms. Blood-smears showed good leucocytosis ; condition rapidly worse ; delirium followed by Cheyne-Stokes respiration and death.

Post-mortem : Abscess in temporo-sphenoidal lobe dry and well

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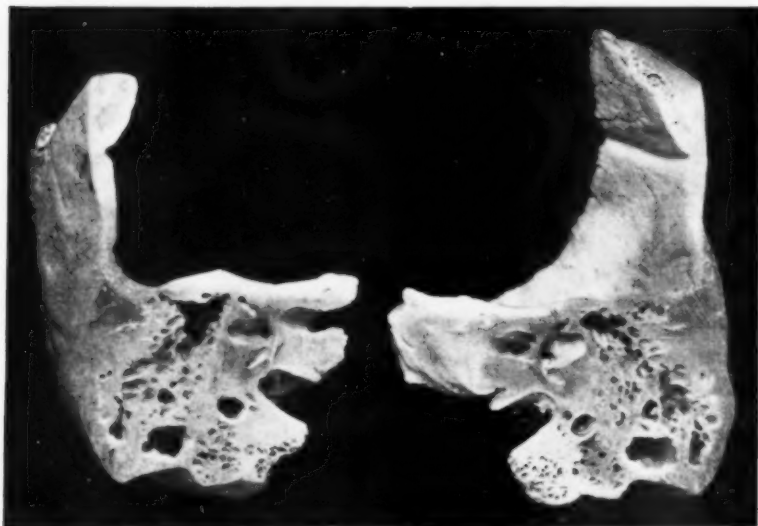
drained; no abscess in cerebellum; basal meningitis (middle fossa); temporo-sphenoidal lobe enlarged, soft, semi-purulent. Spinal meninges not examined.

Dr. DUNDAS GRANT remarked that there was evidence in this case, from the anterior history, that meningitis, if not actually present at the time when the President first saw the case, was already threatening. The fact that the temperature was above the normal was probably due to meningitis commencing and neutralizing the tendency of the cerebral abscess to lead to a subnormal temperature.

A Specimen of Malformation of the Bony External Semicircular Canal, with Photograph.

By ARTHUR H. CHEATLE, F.R.C.S.

THE right temporal bone of a woman, aged 61, who died of melancholia, carcinoma uteri and broncho-pneumonia. The external bony canal is represented by a large smooth-walled cavity opening widely into the outer wall of the vestibule. A small nipple-shaped



The right temporal bone of a woman, aged 61, with malformation of the bony external semicircular canal.

mass of bone projects from the posterior part of the sloping roof. As the deformity was only discovered after drying and cutting, no report could be made of the condition of the membranous canal. The left bone is normal.

MR. JENKINS said this was a type of congenital deformity which one would expect to occur when one considered the development of these canals, which are formed as grooves from the original sac and converted into canals by the fusion of projections from the sides of the groove. It was surprising that such specimens had not come before the Society more often.

An Electric Auriscope.

By P. MACLEOD YEARSLEY, F.R.C.S.

MR. YEARSLEY said that probably all his hearers had sometimes experienced the difficulties of looking at cases where there was not much light available, where the patient was in bed, and one could not get a good reflected light. Recently Dr. Kerr Love showed him an electric auriscope which he had obtained from New York, and which he had used for two years, both for outdoor practice and in the examination of the ears of children. It had given Dr. Love great satisfaction during that time, and Mr. Yearsley liked it so much that he had now got one for his own use. It was not by any means a toy. It could be run by a small "Ever-ready battery." It consisted of a chamber containing a lamp, which was switched on by means of a collar on the handle. There were three sizes of specula which could be fitted in, and a very good view of the membrane could be obtained. Attached was a small lens for magnification, and an arrangement which converted it into a Siegel's speculum. With a shorter speculum and a smaller chamber it might perhaps be used for small operations, such as incising the membrane.

Holmes's Electric Nasopharyngoscope.

By P. MACLEOD YEARSLEY, F.R.C.S.

THIS was the instrument described by Holmes in the *Annals of Otolology, Rhinology, and Laryngology*. It appeared like a Hay's pharyngoscope, but it was passed through the nose, after the fashion of an Eustachian catheter. It moved round in a collar, and was made on

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the principle of a female cystoscope. It produced magnification, and gave a very good view of the nasopharynx. According to Holmes, in a small percentage of cases one could also see the opening of the sphenoidal sinus. Mr. Yearsley regarded it as a valuable instrument, and he had tried it on a number of patients. Very little practice enabled one to recognize the anatomical points in the post-nasal space with great clearness.

DISCUSSION.

Mr. WAGGETT suggested that the operating ear speculum (which was made with the same excellent lens-lamp) was the more valuable instrument, inasmuch as a speculum for use away from the consulting room was usually required for myringotomy. The handle was shorter and thus gave less leverage.

Dr. DUNDAS GRANT considered that the weakest point about the instrument was the long handle, and if it could be made without that, or in such a manner that the handle would not get in the way, it would be better, because the long handle gave such an enormous leverage to the speculum on the walls of the meatus. For examining school children, for instance, it would require more delicacy and gentleness than most people possessed in order to prevent the patient from complaining.

The PRESIDENT suggested that Mr. Waggett might show the instrument he described at another meeting of the Section.

Fluctuating Swelling over Tip of Mastoid and Parotid Region on Right Side in a Case of Chronic Mastoid Disease.

By HUNTER TOD, F.R.C.S.

MALE, aged 48. Admitted to London Hospital, under a surgical colleague, in February, 1903, with chronic middle-ear suppuration and facial paralysis on right side. Schwartze's operation was performed. In October, 1904, the patient came under my care suffering from severe headache, middle-ear suppuration, and a polypus blocking the auditory canal. The complete mastoid operation was performed; there was extensive disease, chiefly involving the tip of the mastoid process and the floor of the auditory canal. The lower portion of the lateral sinus and bulb of the jugular vein were exposed, the walls of which appeared to be healthy. Healing took place rapidly except over the floor of the tympanic cavity. The patient was discharged as an out-patient, but was readmitted again in February 1905, having two sinuses leading down from the old scar towards the tip of the mastoid. The posterior

wound was re-opened and explored, and the bone forming the margins of the jugular fossa, which was necrotic, was removed. The wall of the jugular bulb was perforated, and on enlarging the opening the sinus wall was found to be thickened, and the bulb to be full of granulations. An incision was made along the sinus posteriorly, until bleeding took place, when the plug of gauze was inserted between the sinus wall and the bone, which arrested the bleeding. The patient did well, and was discharged from the hospital, apparently quite healed.

He came up again to the hospital on October 3, 1911, complaining of much pain in the right ear, and a lump which began beneath and behind the ear, and had been gradually increasing in size for the last two or three years. In addition to the fluctuating swelling over the parotid region, the auditory canal is now filled with a large polypus, the pedicle of which is attached to the inferior and posterior part of the canal. Behind the ear is a small sinus from which there is a little purulent discharge.

Apart from this fluctuating swelling, the case is of interest on account of the thrombosis which obviously took place within the jugular bulb six years ago, and which was accidentally discovered at the operation performed in 1905. During no period were there any symptoms of thrombosis, and the temperature throughout remained normal.

DISCUSSION.

Mr. R. LAKE said he regarded it as a parotid tumour, but he was not prepared to specify of what kind. It was probably semi-cartilaginous.

Mr. D. L. SEWELL said he had had very little experience of such tumours, but he thought that the two conditions were not connected with each other, and had arisen independently.

Mr. HERBERT TILLEY remarked that on the previous day he saw a case identical with this, and he agreed with Mr. Sewell that the condition of the ears had nothing to do with the tumour.

Mr. SYDNEY SCOTT said that, whether the two conditions were connected with each other or not, he thought it was important to regard them as separate until an exploration had been made, on account of the risk of infection.

Mr. YEARSLEY said the case reminded him of one which proved to be a dermoid growing under the ear. It fluctuated in size and had a small sinus discharging. He showed the specimen before the Section two years ago, and during the meeting it unaccountably disappeared.

Dr. URBAN PRITCHARD asked if it was a fact that the condition had been noticed only for two or three years, or if, as the patient insisted, it had been coming on for six years—i.e., soon after operation.

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Dr. DUNDAS GRANT said the first thing to do, in his opinion, was to get the ear into as aseptic a condition as possible; and next, to make an exploratory puncture or incision, if necessary, into the swelling.

Mr. HUNTER TOD, in reply, said the swelling had lasted two or three years. He was not certain as to the diagnosis, and he had not removed any portion of the polypus for examination, as he wished the members of the Section to see the case first. Neither could he say whether the swelling was directly connected with the ear or not, but his impression was that the swelling fluctuated, was probably the result of the former ear trouble, and might be a chronic septic affection of the parotid gland. He did not think it was malignant. The chief object in bringing the case before the Society was for opinions with regard to treatment. He proposed to explore the mastoid region and then act accordingly.

Absolute Unilateral Deafness in Children.

By RICHARD LAKE, F.R.C.S.

Case I.—A lad was sent up to me for examination, as somehow or other an impression had been formed that his hearing was not as good as it should be. During the course of an interview with the parents, it appeared that he had passed the physical examination necessary for his admission into one of the Services, but having failed, I presume, in the Arts examination, he was then to be prepared for the sister Service. He proved to be entirely deaf on one side both to osseous and aerial sounds, but he had the extraordinary compensatory development of his sound ear that, however firmly that was closed by means of the finger—his own or his parents'—he was able to repeat sentences at a distance of 14 ft. or 15 ft., this being, unfortunately, the limit obtainable in my consulting room. When, however, Bárány's noise producer was used, one found that he could not hear a loud voice absolutely against the ear. Now, such a compensatory development of his good ear could not have been obtained in a short space of time, and the aural lesion must have existed since earliest infancy.

Case II.—This was a child, aged $4\frac{1}{2}$, more than usually intelligent. This child had been sent up to me the year before, because it had been noticed that she was deaf. There existed the barest trace of adenoids, and I did not consider that their removal would be beneficial. On the second visit, one found that the child's intelligence was sufficiently

developed to be able to proceed carefully with a series of auditory tests, and that she was also mon-aural. I was also informed that at the child's birth considerable difficulty had been experienced, and that forceps had been applied, and it was thought that there had been some facial paralysis on one side, but on which it did not appear to be quite clear.

Case III.—Recently I have seen a third case, occurring in a girl, aged 7. There is no history at all of any injury or illness which could account for the condition. The child is not at all noticeably deaf, except in a noise, when she then employs her good ear, which is the right one. Most careful testing shows conclusively that the left ear is entirely useless, and there is only a suspicion that certain tuning forks are heard on the mastoid on that side. Those are the low-pitched tuning forks, chiefly A, and even these I am not certain of. I inquired particularly from the mother for any particulars as to difficulty at the confinement, but it appeared that the labour was premature, and delivery extremely easy, and the child, though not strong, is well grown and very intelligent. This child, like the others, if she occludes her good ear, or if her good ear is excluded for her by the finger, can hear conversation easily the whole length of the room.

Now the question comes, had the instrumental delivery any direct bearing on the result in the second case. It seems to me that this is quite possible, and that a distinct lesion of the cerebral cortex might have been caused either by direct injury or by intracranial effusion of blood in the temporo-sphenoidal lobe. In none of these children was there any history of illness, nor was there any sign of deficiency in intellectual development, and there was no paralysis or paresis of any other part as far as could be detected.

In these cases I am therefore quite at a loss to account for the condition, but it must be extremely probable that this is due either to intra-uterine disease, or to want of development of the cochlea, and the only means of elucidating the difficulty will be if chance places a post-mortem at our disposal.

DISCUSSION.

The PRESIDENT said these cases opened up a considerable number of problems. In reference to the first case, in which Mr. Lake said his consulting room was 15 ft. long, a very useful method of increasing the hearing distance had been pointed out to him a year ago by Professor Kahn. He had

a small room, and by turning his back to the patient when testing he estimated that he increased the actual hearing distance by one-third; and if he turned the patient's deaf ear towards the wall and he himself stood with his back to the patient the actual distance was increased by two-thirds. He (the President) did not know whether that was scientifically correct, but it occurred to him as a very ingenious observation. With regard to the second case, a very interesting problem arose as to whether injury at birth had anything to do with it. He would like to know whether Mr. Lake had tried the caloric test in this case, because if he could exclude the vestibule from taking part in the trouble there would be much to be said in favour of the view that there had been an injury which had a causal effect. Possibly there was some degeneration of the cortical cells in the hearing centre affecting the cochlear branch of the nerve.

Dr. DUNDAS GRANT said with regard to the idea that a lesion of the cerebral cortex might have produced complete deafness on the opposite side, that he did not think it was possible, because there was so much interlacing of the fibres going from one labyrinth through the auditory nerve to the cortex on both sides. Thus complete deafness could only be produced if the auditory cortical centres on both sides were destroyed. He therefore regarded it as very probable that there had been a want of development or a malformation in the labyrinth in both these cases. With regard to Bárány's "noise-producer," his opinion was that it overdid what was required of it; it might produce apparently complete deafness, when the deafness was not really complete. On the other hand, if the patient heard in spite of Bárány's noise-producer, one might give the patient credit for that amount of hearing, and possibly a little more, and therefore the instrument was of good value.

Mr. SYDNEY SCOTT asked if Mr. Lake had had Wassermann's test done in any of his interesting series of cases. He had a patient, a boy, whose deafness had been attributed to adenoids. A careful examination, however, showed that he was absolutely deaf in one ear, and very slightly deaf in the other. The result of applying the caloric and rotation tests was negative on each side. The reactions indicated that both vestibular organs and one cochlea were defunct, so that he had only one cochlea left. Wassermann's reaction was definitely positive. He wondered if any of Mr. Lake's cases were similar to this.

Mr. LAKE, in answer to the President's question, said he feared he had not a good opinion of the value of the tests, and was waiting for someone to show him their real value. With regard to the question of the cerebral cortex, in reference to Case II he used the term in a vague way. He meant injury to the brain as being a possible explanation. He had not done the Wassermann test in any of the cases, and did not think any of them showed signs of syphilis.

A Note upon the Treatment of Cholesteatoma.

By RICHARD LAKE, F.R.C.S.

THE essential to be aimed at in the cure of the above condition being to obtain absolute dryness, it became necessary to consider carefully whether treatment with alcohol is calculated to obtain such a result. The reasons which militate against this form of treatment are, that, in the first place, alcohol rarely of itself, however carefully applied, results in a cure; and, secondly, that alcohol evaporates less readily than it absorbs water, and that unless the alcohol be entirely absolute, or as nearly so as can be commercially obtained, it contains already a certain amount of water, which must be left behind, if the alcohol can be entirely evaporated. It seemed necessary, therefore, to seek further. The only fluid which apparently fulfilled the requirement was ether, and after some years of trial ether has in my hands apparently acted in the way in which it was hoped it would. Ether, like alcohol, causes a certain amount of local discomfort, but the burning and pain are less in intensity and more evanescent. The method of applying ether is to take a probe armed with cotton-wool saturated with ether, and to thoroughly swab out the disease area. When this is done by the medical man himself very rapid drying can be obtained by blowing gently into the ear with a rubber bag (Politzer's). The patients themselves can easily carry out this treatment, but they should be seen at intervals for the surgeon to remove any dry fragments of the mass which have not come away on the swabs.

Case of Sarcoma of the External Ear.

By RICHARD LAKE, F.R.C.S.

THIS patient, a sailor, aged 71, came to the hospital complaining of a growth on the right external ear; it had been present for four months, having started as a small pimple; it had been rapidly increasing in size; for the last two months there had been frequent and severe hæmorrhages. There was no pain. On examination the growth was found to be springing from the upper part of the auricle, and had not extended into

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the external auditory meatus. There was no glandular involvement. The growth was found on microscopical examination to be a mixed spindle- and round-celled sarcoma. The growth was removed, the wound healing by first intention.

There was a history of injury dating back seven years, at which time the patient was struck on the ear by a block, causing a sore which never healed, as he was constantly picking it.

DISCUSSION.

Mr. SYDNEY SCOTT thought the condition must be very rare, and it would be interesting to hear whether other members present had seen many cases of sarcoma of the pinna. He had seen only one other.

Mr. MACLEOD YEARSLEY said a case of melanotic sarcoma of the pinna, occurring in a girl, aged 11, had been published by Stowers.¹

The PRESIDENT said it must be a very rare condition: he had seen only one case of the kind.

A Case of Hysterical Deafness Diagnosed (and Cured) by the Caloric Vestibular Test.

By DAN MCKENZIE, M.D.

THE events in this case dramatically exemplified the value of the vestibular tests in the diagnosis of hysterical deafness. The patient, a middle-aged woman, had been very deaf in the right ear since childhood and had depended entirely upon the left ear, the hearing power of which had been very good until two months before she came to hospital, when it began to disappear—gradually—she said. The hearing tests worked out as follows:—

	Right				Left			
Whisper	— ∞	— ∞	...	
Conversation	?	6 inches	...	
Tuning fork (256) :—								
Meatus	— ∞	— ∞	...	
Mastoid	— 5 seconds	— 5 seconds	...	
Weber	?	?	...	
Rinné	—	—	...	
Galton	4	2.2	...	

¹ *Brit. Journ. Derm.*, 1893, v, p. 305.

The right membrane showed scars; the left an old perforation.

There was nothing in the case, so far, to suggest hysteria, and indeed it was looked upon as an instance of labyrinth degeneration supervening upon old middle-ear disease, the only point of interest being the comparatively recent involvement of the left labyrinth. In order to ascertain the condition of the vestibular sense the cold caloric test was applied after the manner I usually adopt—i.e., measuring the induction period. In the right ear a very slight nystagmus appeared in 60 seconds (normal = 25 to 35 seconds), and only very trifling vertigo was experienced. In the left ear, on the other hand, marked nystagmus appeared in 25 seconds, with vertigo, and a sudden outburst of tears and sobs. When this had subsided, the patient declared that she could hear, and on examination it was found that the whisper could now be heard in the left ear at a distance of 24 ft., while in the right ear the hearing remained as before.

The patient then volunteered the information that she had several times lost her voice, and had had it restored "by the battery." And there can be no doubt that it was the memory of this previous successful treatment, coupled with the profound mental shock of the violent vestibular stimulation, which cured her deafness on this occasion.

The contrast between the vestibular reactions in the two ears obtained at the same sitting in the same patient is sufficiently striking to require no comment.

I do not know whether it has been observed that hysterical deafness usually appears in people who are already rather hard of hearing; presumably the existence of the slight deafness supplies the suggestion.

DISCUSSION.

The PRESIDENT said he would take exception to the last paragraph in the notes. He had not seen many cases of hysterical deafness, but he could recall several where there had been no previous deafness at all.

Dr. MCKENZIE, in reply, said he had seen three or four cases of hysterical deafness in the last two or three years, and in all of them there was a history of previous deafness. Then the hysterical deafness came on and made the patient absolutely deaf, and after the hysterical deafness passed off there was some degree of deafness still remaining. Perhaps it was too strong a statement to apply the term "usually" to what was, after all, merely a personal experience.

A Case in which the Cure of Constipation induced the Disappearance of Aural Vertigo (Mènière's Syndrome).

By DAN MCKENZIE, M.D.

ON a previous occasion¹ I showed a case in which severe aural vertigo of the Mènière type underwent benefit as a result of vegetarianism and iodide of potash. In order to complete the record of that case I take this opportunity of noting that the patient's attacks entirely ceased after six months' treatment. He is now quite well, and has returned to work, and is still a vegetarian. In the present patient the symptoms were similar but much less severe. And here, also, dieting, albeit of a different kind, has abolished the attacks.

The patient, a man, aged 30, came to hospital complaining of tinnitus in the left ear. The hearing tests show the signs of slight nerve-deafness. They are as follows:—

Tuning fork (256)			Right ear			Left ear		
Meatus	±	—	4	
Mastoid	±	—	3	
Weber lateralized to right.								
Rinné	+	+		
Galton	2·5	3		

Vestibular tests: Right ear—nystagmus in 30 seconds; rather small movements; no vertigo. Left ear—nystagmus in 25 seconds; vertigo.

On running over the nervous system nothing was found to explain the on-coming nerve-deafness; and the middle ears seemed to be healthy. But on going into the history the following facts came to light; Nine years ago he began to suffer from recurrent attacks of vertigo and vomiting. The intervals between the attacks were prolonged at first (eighteen months, six months, &c.), but became gradually shorter as time went on; they were never frequent, however. A man of unusual intelligence, he describes his attacks at once concisely and vividly. The first symptom observed was tinnitus in the left ear. This was followed in about half an hour by deafness

¹ *Proceedings*, 1910, iii, p. 50.

in the same ear and vertigo so violent that he had to lie down. Sickness and vomiting followed, and then the whole of the unpleasant phenomena rapidly disappeared. There was no loss of consciousness. These attacks recurred at intervals during a period of seven years. For the last two years he has not had any return of them, and it would seem from his replies to careful questions that the disappearance of the attacks coincided with the cure, by means of appropriate dieting, of the constipation from which he suffered. It is noteworthy that he applied himself to the cure of his constipation in order to put a stop to periodical hæmorrhage from hæmorrhoids. There is probably no direct causative link between the hæmorrhage and the vertigo, for he states positively that the vertiginous attacks preceded the appearance of the bleeding in point of time.

During the last two years the tinnitus has become persistent.

With regard to the pathogenesis of this train of aural symptoms, we may assume the influence of a gastro-intestinal toxin acting either upon the nerve-endings within the labyrinth or upon the nerve-centres. The later appearance of persistent tinnitus with nerve-deafness favours the supposition that the site of the lesion—whatever that lesion actually may have been—was in the labyrinth, and not in the central nervous system.

Such cases as these show that what popularly pass as "bilious attacks" are, at times, the occurrence of the labyrinth storm, known as "Ménière's syndrome."

Meatal Exostosis, and Patient after Removal.

By C. E. WEST, F.R.C.S.

MALE, aged 26. Left meatus was completely blocked $\frac{1}{2}$ in. within the opening by a fixed, hard, pink mass, somewhat lobulated on the surface. It was not tender, but was sensitive to touch. Symptoms: deafness and pain, apparently due to pressure. Operation (September 27): through post-aural incision. The growth was detached *en bloc* by the gouge; its attachment was to the outer edge of the tympanic plate below and to the floor of the bony meatus for about a $\frac{1}{4}$ in. After removal a small attic perforation with cholesteatoma was visible. The outer attic wall was removed and a graft introduced into the meatus.

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The specimen is a somewhat nodular mass of bone, measuring 16 mm. by 10 mm. at its base and 10 mm. in height. The surface of section seems to be closely cancellous.

The patient may be fairly called an infrequent bather.

DISCUSSION.

Dr. PRITCHARD said he would like to know if the exostosis could have been broken off with a pair of dental stump forceps. Although apparently the attachment was much larger than usual, he thought it was one of the cases of single exostosis which were totally different from the ordinary ones, and which had usually a very small attachment.

Mr. WAGGETT recalled a case of exostosis in which this apparently trivial condition resulted in a fatal issue. The patient met his death through falling into the fire, presumably in an attack of vertigo.

Dr. DUNDAS GRANT said exostoses should be distinguished from hyperostoses. Pedunculated exostoses were usually so small that they could be extracted through the meatus, and on more than one occasion he had removed them by means of Hovell's plan—boring a hole into the exostosis and inserting a screw with a handle to pull it out. But on one occasion he tried to do this, and failed on account of the shape of the exostosis. It was almond-shaped and extended a long way downwards, making a space for itself below the level of the floor of the meatus. It could only be removed by means of a post-aural incision, through which it was got out with ease.

The PRESIDENT said that in discussing the question a sharp line should be drawn between exostosis and hyperostosis from the points of view of both aetiology and treatment. Not long ago he was criticized by members of the Section for making the remark that exostosis was a rare disease in the ear, being assured that it was very common in the South. He did not think it was common in the North.

Case of former Chronic Suppuration with Epileptiform Attacks.

By J. DUNDAS GRANT, M.D.

Dr. GRANT said that the fenestra ovalis was freely exposed, and a small, white, irregular granule of bone was seen at the upper part of the promontory. It was probably a portion of the dislocated stapes. Ossiclectomy was done four years ago. He wished to ask if those who examined the case were as convinced as he was as to the nature of the

parts seen. The fenestra ovalis was closed inside by a membrane, and he would like to know if this was the membranous utricle, and if the nodule was a portion of the stapes. He would contribute a full history of the case at a later meeting.

DISCUSSION.

Dr. H. J. DAVIS considered that the spicule of bone seen was the footplate of the stapes.

Dr. GRANT, in reply to Mr. Cheate, said he had not looked at the case that afternoon, but he saw it in the morning; the features of it were then quite distinct, and there was practically no moisture. There was a shining surface of bone, with a very thin membrane on the surface. In agreement with Dr. Davis, he thought the spicule was a portion of the stapes; he did not know whether it was the footplate.

Note of a Case of Epithelioma of the External Ear.

By G. N. BIGGS, M.B.

THE patient was sent to the hospital on account of a small growth on the upper part of the right auricle, which had been present for eight weeks. It was rapidly increasing in size. The patient complained of no other symptoms. On examination, a small hard mass was found on the upper part of the pinna. A piece was removed for microscopical examination, and was found to be an epithelioma. There was no glandular involvement. The growth with the upper part of the pinna was removed, the wound healing by first intention.

Case and section shown.

Notes of a Case of Temporo-sphenoidal Abscess and Meningitis following Middle-ear Suppuration.

By G. N. BIGGS, M.B.

TWENTY years ago the patient had had discharge from both ears, the left being the worst; at that time the patient was very irritable and had frequent severe headaches on the left side. Twelve years ago the discharge in both ears ceased, and the patient has had no headaches

or any other symptoms from that time. Seven days ago he was seen, complaining of severe pain in the left ear of seven days' duration. On examination the membrana tympani had been found to be bulging, and had been incised.

Seven days later he was brought to the hospital, and came under my care for the first time, his wife stating that for four days the headache and pain in the ear had been unbearable, and that for the last two days he had been delirious. A careful examination of the patient was quite impossible owing to his great restlessness. At intervals he cried out, and held his head as if in very great pain. Temperature, 102.4° F.; pulse 100 and slightly irregular. Tache cérébrale was easily elicited.

An immediate operation was undertaken, with the hope that if the meningitis was in an early stage an attempt might be made to save him by drainage through the labyrinth. Under the anæsthetic a lumbar puncture was performed, when it was found that the cerebro-spinal fluid was under pressure, and was turbid. The eyes were also examined; optic neuritis was found to be present on the left side, there was also engorgement of the vessels on the right side. The operation revealed the presence of pus in the labyrinth, and a much too extensive meningitis for any operative interference.

Three days after the operation the patient died.

At the post-mortem examination a very interesting condition was revealed. The patient had died from an extension of the disease through the labyrinth and internal auditory meatus. Cultures from the pus in the middle ear, labyrinth and base of the brain revealed the same organism. The convolutions over the left temporo-sphenoidal lobe were seen to be much flattened, but otherwise quite healthy. On section of the brain, however, a very large temporo-sphenoidal abscess was revealed, the walls being very thick. A bacteriological examination of the contents proved them to be sterile.

Evidently the abscess dated from the middle-ear disease twenty years previously, the abscess becoming encapsuled and the middle-ear suppuration ceasing. The case is interesting, as it is, I think, rare to find a case developing a severe intracranial lesion secondary to middle-ear suppuration recovering, only to fall a victim to a different intracranial lesion secondary to a second attack of middle-ear disease. The man was a boxer, and had been fighting regularly for the last twenty years or more.

Otological Section.

November 17, 1911.

Dr. W. MILLIGAN, President of the Section, in the Chair.

Carcinoma of Middle Ear.

By W. MILLIGAN, M.D.

PATIENT, male, aged 31, had suffered from suppurative middle-ear disease (right side) since 4 years of age. Four months previous to coming to hospital he received a blow over occiput and mastoid process of right side, which was followed by severe pain and headache. Upon admission right meatus was found filled with a greyish-looking, sloughy polypus. Marked tenderness, but no œdema over mastoid process. Temperature 99.2° F.; pulse 82. Tuning forks lateralized to right ear. No nystagmus, optic neuritis, or facial paralysis.

Diagnosis: Malignant disease of middle ear (?); exploratory operation suggested.

Operation: Mastoid cortex removed. Cells full of vascular granulation tissue and pus; two small sequestra removed. Dura over base of temporo-sphenoidal lobe found exposed and covered with granulation tissue; growth springing from tympanic mucosa. Wound behind ear left entirely open. Great relief from pain and headache. Rapid recurrence of growth and development of facial paralysis.

Death from exhaustion four months after admission to hospital.

Microscopic report: "A true epithelioma; cell-nest formation well marked."

Carcinoma of Middle Ear; Facial Paralysis.

By W. MILLIGAN, M.D.

PATIENT, female, aged 64. Left ear had discharged since infancy. No pain or discomfort until three months before admission to hospital. No history of injury. Admitted to hospital complaining of severe pain over left side of face. Left meatus full of friable and vascular granulation tissue. No nystagmus; no optic neuritis. Tuning forks lateralized to affected side. Facial paralysis well marked. Portion of growth removed for microscopic examination.

Microscopic Report: "Section shows irregular masses of squamous epithelial cells, with some attempt at 'nest' formation. Very little supporting connective tissue seen. The tissue appears to be a portion of a rapidly growing squamous-celled carcinoma, but the absence of normal tissue showing invasion makes it impossible to be quite certain."

Gradual increase of pain. Removal of mastoid cortex suggested. Mastoid cells found full of growth extending backwards to lateral sinus, which was exposed, and forwards into zygomatic area. Invasion of exposed dura mater over roof of middle ear and mastoid antrum. Growth scraped out as completely as possible. Wound packed and left completely open. Great relief from "pressure pain." Rapid recurrence of growth. Patient since lost sight of.

Patient Four Years after Operation for Carcinoma of the External Meatus and Tympanum.

By C. E. WEST, F.R.C.S.

OPERATION, November 25, 1907: Removal of whole of cartilaginous and bony meatus, together with pre-auricular and mastoid superficial tissues and lymphatic glands. Extended radical mastoid operation. No recurrence. Squamous-celled carcinoma. Patient's external auditory meatus also shown with growth in situ.

DISCUSSION.

The PRESIDENT (Dr. W. Milligan) said he recorded his cases in order to elicit opinions as to whether traumatism had anything to do with the production of malignancy in the middle ear; or as to what might be the reason of a septic process becoming malignant in the course of years.

Mr. C. E. WEST said there were one or two points of great interest in Dr. Milligan's cases. The first was the great frequency with which carcinoma, so-called of the middle ear, was found, on examination, to be of the squamous-celled variety; absolutely typical, and looking on section like ordinary carcinoma of the tongue or lip. In February, 1909,¹ he exhibited a group of cases before this Section, in each of which the microscopical report was that it was typical squamous-celled carcinoma. He believed these present cases were not, properly speaking, carcinomata of the middle ear, except perhaps by extension, and that they originated in the deeper part of the external auditory meatus. He based this belief on two considerations: first, the histological character, which was nearly always that of squamous-celled carcinoma; and secondly, that he had seen a case of carcinoma which involved the meatus only—i.e., it had not penetrated the tympanic membrane at all. Otherwise, the growth was exactly like other growths that had penetrated the tympanum and involved the mastoid. With regard to the two points raised by the President—the influence of injury in connexion with such growths, and the influence of septic processes—his own personal experience was so small that it was impossible for him to judge on a statistical basis from his own cases, but in a large number of cases attention was drawn to the occurrence of some accident to the head. Taking the first case, it was difficult to see how a blow on the occiput could produce malignant disease of the tympanum by any process of genetic connexion. He thought that when the patient found anything wrong with his ear, his ætiological conscience was aroused, and he sought for a cause for what had happened, and he would remember that he ran his head against the bedpost three weeks ago, or something of the kind. But, on the other hand, there was strong ground for thinking that the continuance of septic processes had a very important bearing on the genesis of malignant disease. In these cases there was often a history of prolonged middle-ear suppuration: and though in some of them the suppuration was probably only secondary to the ulceration of the growth, in the majority the suppuration was antecedent to the growth by many years. In that connexion he wished to point out that the site at which the growth commenced, which he believed to be in the floor of the deepest part of the meatus, was precisely where pus would lie in a pool during the whole course of the chronic suppuration. If one looked at malignant disease in other situations he thought that there again one saw the frequent coincidence of septic processes with the development of carcinoma. Only on

¹ *Proceedings*, 1909, ii, pp. 34 and 87.

the previous day he had occasion to take a case across to another department because he discovered that there was an ordinary carcinoma, squamous-celled no doubt, growing on the mucous reflection on the side of the tongue, far back. That patient had a most hideously septic mouth and teeth. He believed that nearly all patients with carcinoma of the tongue had very septic mouths.

Dr. FITZGERALD POWELL said he thought that suppuration could not be looked upon as a causation or factor in the production of malignant disease of the ear, but that, as in other cancers, suppuration no doubt aggravated and increased the rapidity and extension of the growth, and this, he thought, was caused by the irritation of the cells by being bathed in the foul discharge, not by any specific action of the septic organisms. It was difficult to believe that a blow on the side of the head should so devitalize the tissues as to be a cause of the development of malignant disease in the ear. Irritation of the part, he thought, was a much more reasonable suggestion.

Dr. DUNDAS GRANT remarked that in both the President's cases great relief followed the operation. He had seen such relief himself from partial measures, and he thought one should not be deterred from doing so much by the fact that the diagnosis of malignant disease had been arrived at.

Dr. PRITCHARD also desired to emphasize what Dr. Dundas Grant had said. He had known a number of cases in which it was not certain before operation that disease was malignant, where on operating the pain was absolutely relieved, as in the President's cases.

Mr. SYDNEY SCOTT said that, in his opinion, the surgeon should not be satisfied with a small and partial operation in such cases; but when it had been recognized that the disease was malignant, the widest possible operation which it was safe to carry out should be undertaken. In such a case he would not limit the operation to the ear itself, but would go further, and do what others had done in cancer of the throat and tongue—namely, remove the glands in the anterior triangle of the neck. In other words, follow out the principle of Butlin's operation in cancer of the tongue.

Mr. A. CHEATLE thought members must be prepared to accept Sir Henry Butlin's conclusion with regard to cancer—namely, that it was due to a parasite. With regard to operations for carcinoma, it was his experience that when the middle ear was involved, nothing would save the patient.

Dr. E. LAW said that suppuration of the middle ear was very common, and he would be glad to hear if any member had ever kept under observation a case in which carcinoma followed as a complication. He had not himself directly seen carcinoma following suppuration, but had only heard of it from the patients.

Mr. C. A. BALLANCE said the question of the influence of trauma on the occurrence of malignant disease was a very important one, and he thought one must look upon it as only a partial cause of the disease. Just as when one met with a case of tuberculosis of the knee-joint the patient would say

that six months previously he had strained the knee or received a blow on it, so in malignant tumours there was generally a history of trauma given. Trauma might influence the soil in favour of the growth of cancer, but it could be nothing more than a partial cause. He had been much interested in Mr. West's case of operation on a case of carcinoma of the external meatus and tympanum, in which there had been no recurrence. Mr. West said he had dissected out the facial nerve and removed all the diseased bone. He referred to a similar case, but he did not obtain such a good result. Three or four years ago he saw a gentleman with an ulcer on the upper part of the pinna, which he took to be rodent ulcer. There were no glands involved, and the edge of the ulcer was not hard. He took away part of the pinna for examination, and Mr. Shattock reported that it was typical squamous-celled carcinoma. He did not see the patient again until the beginning of last April, when he presented himself with the complaint of itching in the meatus. During the last six weeks this had kept him awake at night. There was no discharge and nothing could be seen in the meatus, though it was a little swollen: the canal of the meatus on that side was not so large as that on the opposite side. No lymphatic glands were enlarged. The patient said he was going to Homburg the next day, and he told him to go, but suspected that there would be a recurrence. He heard nothing further of the patient until the middle of July, when he learned that he was well until May 15, at which date he had a very severe pain in the ear and called in a Homburg surgeon. That surgeon gave him hot fomentations, and after a few days, incised the drum, but nothing came out. He believed the incision was repeated every day thereafter for a week, and at the end of a week pus came out, but the pain was not at all relieved. At the end of two or three weeks from the commencement of the severe pain—so severe as to require morphia—the surgeon called in another surgeon and they decided that a mastoid operation must be done. By this time some pus was coming away from the meatus. A small incision was made over the mastoid, the mastoid process was opened, and then it was decided it was of no use to go on with the operation. He had a letter explaining afterwards this was because there was a tumour inside the mastoid. He saw the patient when he returned on July 15 (he had been so ill with the pain that he had not been able to travel before the date). He then had an enormous swelling over the left ear, and foul pus was oozing from the meatus and from the incision over the mastoid, and almost the whole of that side of the head was œdematous. He made a very free incision, taking away the cortex of the mastoid, and found the cavity of the mastoid filled with foul pus and pinkish tissue. In front of the ear there was a swelling as if the pre-auricular gland was enlarged. There were no enlarged glands in the neck. He removed the whole of the disease. The disease had completed the "complete" mastoid operation, and all he had to do was to scrape the cavity out and remove all the bone he could get hold of. He had not to think about the facial nerve as that had been already destroyed. For six weeks the patient was free from pain; but when Mr.

Ballance came back from his holiday at the end of September he was in great pain; the wound, which had been left open, had partly closed, and the huge cavity in the bone was again filled with pinkish material. It was all quite sweet, as the cavity had been treated daily. He thought that the only way to deal with it was to remove the material again, and he scraped it all out. But the relief from pain on this occasion lasted only a fortnight. The pain returned, and there were still no enlarged glands in the neck, but the edges of the wound became infected. He had the growth examined and it was pronounced to be typical squamous-celled carcinoma. In front of the ear there was very considerable swelling, and he cut into that because it seemed to be partly fluid, but it was not so. He took a piece out and had it microscoped. This also proved to be typical squamous-celled carcinoma with nests. He was having terrible pain from it, for which 3 gr. or 4 gr. of morphia a day were given. He did not know what further could be done, but suddenly something occurred which made him think something else might be tried. He met in London Dr. Coley and asked him if he could do anything for his case. The answer was that if his fluid were used, the pain would be taken away. He told Dr. Coley that the man was so bad—there was twitching of the arm on the opposite side, so that the disease had probably affected his dura—that he (Dr. Coley) had better come and inject it himself. Mr. Ballance did not then think the man would live more than a few days. Dr. Coley consented to come, and injected him with small doses of his fluid for a week, and then used a larger dose. After this he had an appalling rigor, lasting all night, during which it was thought he would die. But from that time he had had no pain at all. On the present day he was out for a drive, was taking his food well, and the lumps in front of and behind the ear had almost disappeared. He did not wish members to think that the Coley's fluid had brought about a cure, but it had certainly taken away the pain, and if any of his hearers had a case of carcinoma of the ear in which there was great pain, he could strongly recommend the use of Coley's fluid. Whether the present patient would also be cured of his tumour he did not know, but he was apparently well and most of the tumour growth had disappeared. Sir Henry Butlin said certain cases of cancer did get well without anything being done, and this might be such a case, or the improvement might be due to Coley's fluid. He would also like to mention another case of great interest which he had had this year. A woman came from abroad with an appalling degree of epileptiform neuralgia. He discovered that she had a foul discharge from the ear, which she had had ever since she was abroad. He thought probably the temporal bone suppuration had extended to Meckel's ganglion, and had involved the fifth nerve. He did the ordinary operation and then found that the dura mater was adherent to the bone. He took away some of it and found that the meninges were adherent over a considerable distance, certainly to the cave of Meckel. She had clearly a meningitis which extended to the cave of Meckel and produced the neuralgia. He thought she would get well, for she was much

better for some time. But the pain had now partly returned, and she was now evidently going downhill. About a month ago it was noticed that she had paralysis of the sterno-mastoid on that side, and that was a new symptom. Skiagrams also appeared to show sarcomatous destruction of bone. He thought the area of suppuration which caused the attack of meningitis had become malignant. So that this was an illustration of old chronic suppuration, which had not only caused great distress, involvement of the fifth nerve, and pachymeningitis, but had become a malignant tumour of the temporal bone. Otherwise he did not know how it was possible for the spinal accessory nerve to be involved.

The PRESIDENT congratulated Mr. West upon the result in his case. He read a letter which he received from Dr. Wilkin, in which he said that the rarity of those cases, coupled with their practically hopeless course, led him to mention one under his care. About two months after the patient had been knocked down in the street, being much bruised about the head, the ear being particularly affected, he went to the Westminster Hospital complaining of great pain in the ear, and later came under Dr. Wilkin's care at the London Throat Hospital. He removed a portion of the growth and had examined; the report was that it was a squamous-celled epithelioma. Seeing an operation would be hopeless, he applied von Mosetig's pyoktanin treatment. He found that it relieved the pain and constant discharge. Post-mortem examination, however, showed that the growth had involved the whole of the bone down to, but not touching, the meninges. The effect of the treatment, was first the great relief from pain, and secondly the conversion of a foul discharge into a non-smelling one. He began with a one-five-hundredth solution, and worked up to one-three-hundredth. Post mortem, the lymphatics were for some distance stained and knotted up. That was suggestive in connexion with its use in breast cases. The President thanked members for the valuable hints they had given. He did not wish them to think that his impression had been that the blow was actually responsible for the carcinoma, but he thought that the trauma might have aggravated it. The cases he had seen had, according to the history, all followed prolonged suppuration of the middle ear, but he could not say he had seen such a case develop under his own eyes. With regard to the general question of sepsis, he looked upon it as a very distinct ætiological factor; indeed, he regarded it as a sort of trauma. With regard to operation, in neither of his cases did he think the growth could be removed. Although the idea of wide operation was of course entertained at the time, it did not seem feasible on consideration; and he therefore contented himself with removing the cortex, which procedure, as Dr. Grant remarked, afforded very marked relief from pain. He remembered the cases which Mr. West showed before the Section, and that the point was raised at the time whether they did not arise in the deeper portion of the epithelial covering of the auditory meatus and extend inwards. He could not say whether that was so in his cases. The whole of the tissues were so involved in the growth that it was practically impossible to make it out. He had been much interested in hearing Mr. Ballance's remarks on the value of Coley's fluid. Dr. Milligan

32 Cheatle: *Rare Form of Diploëtic Type of Temporal Bone*

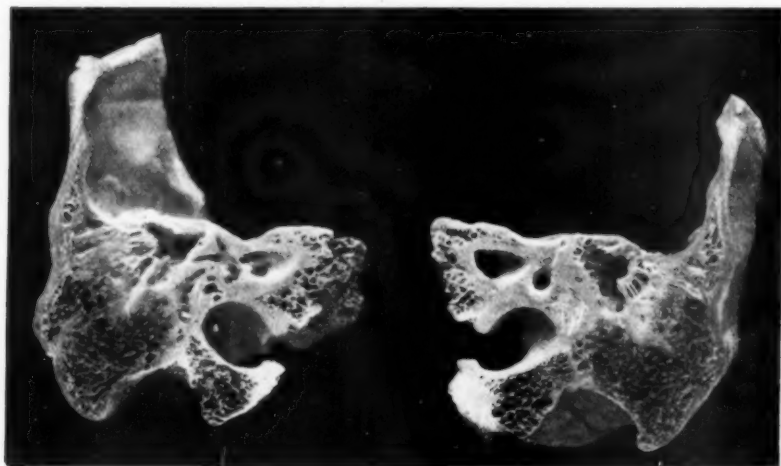
had tried it; it had produced rigors, as in Mr. Ballance's case, but he had never seen any benefit result.

Mr. WEST, in reply, apologized for not being able to provide a specimen. This was in existence a few months ago, but had disappeared.¹ It was the external meatus split longitudinally and showing the growth, a white mass, passing finger-like processes into the deeper tissues, just like squamous carcinoma of the tongue. He had been asked what he did with the facial nerve. With Mr. Scott's assistance, he dissected it out from the geniculate ganglion to the stylo-mastoid foramen, the loop being held forward on a bent probe, and the deeper parts of the growth, which had extended into the sinus tympanicus and down to the facial nerve, were freely removed with a gouge and hammer. When he thought he had got to the end of it, the nerve was put back into its place. Of course the patient had facial paralysis, but this cleared up later, so that six months after the operation he was in his present condition.

A Rare Form of the Diploëtic Type of Temporal Bone.

By ARTHUR H. CHEATLE, F.R.C.S.

THE temporal bones are those of a man, aged 33, who was a congenital imbecile and who died of mania, broncho-pneumonia, and heart



Left temporal bone, showing the distribution of the diploë.

¹ Since the meeting the missing specimen has been found and is preserved in the Aural Department at St. Bartholomew's Hospital.

failure. Left bone: The outer wall of the antrum is diploëtic, and measures half an inch in thickness; the diploë is separated from the foetal cells by a thin layer of dense bone. The section shows the three masses of diploë belonging to the zygomatic, squamous, and petrous elements to be separated from one another by distinct but thin layers of compact bone.

Right bone: This is somewhat similar, but the squamous and petrous masses of diploë are not marked off from one another, and the compact layer separating the zygomatic from the squamous diploë is thick and forms a dense outer wall to the antrum. A few cells run downwards from the apex of the antrum.

Mr. CHEATLE said this was a rather rare form of temporal bone, the rarity consisting in the amount and distribution of the diploë. It explained the cases of suppuration which ran an osteomyelitic course.

Case of Residua of Suppurative Otitis; frequent Epileptiform Attacks which ceased after Ossiculectomy; Labyrinthine Tests.

By J. DUNDAS GRANT, M.D.

MR. I., aged 34, was first seen by the exhibitor on December 13, 1906, complaining of sudden attacks of giddiness or loss of consciousness, and dullness of hearing in the left ear. He had been subject to attacks of dizziness for about four years before he came, and during the last two years had had attacks of vertigo with loss of consciousness. The attacks were of two kinds: one preceded by a feeling of pressure behind the ear, after which he fell over, and the other with absolutely no warning at all, in which he suddenly fell right down, with loss of consciousness. The attacks came on about three or four times a week. He had had deafness in the left ear since the age of 8 or 9, but never remembered having had a discharge.

On examination there was seen a depression corresponding to a perforation behind the malleus, in which the stapes was visible, with a sunken cicatrix attached to it; it was then noted that there was giddiness when Siegle's otoscope was employed.

He was at first treated with spirit drops, and on March 1, 1907, the exhibitor performed ossiculectomy; from that time he has been entirely free from the attacks. The fenestra ovalis was plainly visible and

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closed by a thin, shiny membrane. A small white granule of bone—a portion of the dislocated stapes—was seen on the upper part of the promontory, below which was the niche for the fenestra rotunda.

The rotation tests are practically normal, and are in either direction accompanied by vertigo. The caloric test was not employed, as there was ample evidence that the labyrinth was active and the injection of liquids offered a risk of re-awakening a former suppuration. The tuning fork tests are as follows: Galton's whistle is heard in the left ear up to 6, but with noise machine in the right ear only up to 9; the tuning fork on the vertex is heard better in the left ear; bone-conduction is normal in both ears, and Rinné's test positive in the right ear and negative in the left.

The patient was shown at the last meeting.¹

DISCUSSION.

Dr. GRANT added that with regard to the "fistula test," it was difficult to say what nystagmus was produced. There was an irregular rotation of the eye, but he had not been able to determine its direction. It was suction which produced it most, and possibly it produced a complex form of nystagmus, such as would not be seen in fistulae of the external semicircular canal. It must act on all the semicircular canals together. That seemed a reason why the direction of the nystagmus should be so indefinite. The attacks had been looked upon as epileptic; and he regarded them as explained by peripheral irritation in the middle ear on a healthy, or perhaps over-sensitive, labyrinth. In answer to a question by the President, he said there was no definite auditory aura, but in one kind of attack the patient was conscious of a feeling of pressure behind the ear before the attack came on. In the other kind of attack the patient had no consciousness of any aura at all; he simply dropped down, and was sure his loss of consciousness was complete.

Dr. DAN MCKENZIE said probably most of his hearers would remember, in connexion with this case, an interesting lecture by Sir William Gowers five or six years ago, entitled, "The Borderland of Epilepsy." In that lecture attention was drawn to a series of cases in which there was an indefinite, ill-defined type of epileptiform attack. The feature which struck him most was that in many of the cases vertigo was a prominent symptom. It was well to recall what was said in that lecture, and associate those unexplained symptoms with recent work on the labyrinth. It was possible that some, at least, of those cases originated, as this case did, in a diseased condition of the labyrinth. If that were so, the possibility also existed that one might be able to relieve or cure many of them by a comparatively simple operative procedure. It was desirable to point out that a diseased labyrinth might be hyper-active.

¹ See *Proceedings*, p. 22.

Dr. DUNDAS GRANT, in reply, suggested that the indications in this case were that the labyrinth was healthy. There seemed to have been an abnormal looseness of the stapes, and the impact of that stapes upon a healthy, or at all events only a hyper-sensitive, labyrinth, would account for the symptoms.

Case in which a Cholesteatoma "performed" the Radical Mastoid Operation.

By W. M. MOLLISON, M.C.

W. B., AGED 19, was admitted to Guy's Hospital on July 18, 1911. He had suffered from otorrhœa from the right ear for eight months; he had had no pain but was occasionally giddy. Five weeks before admission an abscess formed behind the right ear and burst, and has discharged continuously since.

On admission there was a sinus over the right mastoid, discharging pus, and otorrhœa from that ear. The left ear was operated on five years ago and is still discharging. At the operation on the right ear the whole mastoid was found to be filled with a cholesteatomatous mass; on removing this a cavity was seen imitating that produced by a surgeon in performing the radical operation. The walls of the cavity were beautifully smooth; the facial ridge was reduced to the smallest amount compatible with safety to the nerve. The disease had exposed the dura mater of the middle fossa over a small area, and over the lateral sinus was exposed a small patch of pachymeningitis. There was a fistula in the anterior part of the external semicircular canal into which a small probe could be passed, and the facial nerve was lying freely exposed for $\frac{1}{2}$ in. above the fenestra ovalis; on touching the nerve the face twitched (after operation no trace of paresis).

The membrane (epithelial) lining the cavity was scraped away and the fistula in the external canal was enlarged with the electric burr and bone removed just round the patch of pachymeningitis, a meatal flap cut, and an incision made through the crus of the helix, and a tube put in the meatus. Recovery uneventful; no vertigo or headache, though for three days after operation there was slight rotatory contralateral nystagmus.

Seen again on October 10: The whole cavity was quite dry. Hearing of 4 ft. to conversational speech; upper tone limit depressed

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to 14,000 vibrations per second (Edelmann-Galton whistle). No spontaneous nystagmus, no vertigo. Caloric reactions (head upright): in right ear reaction in fifteen seconds, lasted two to three minutes; in left ear much the same, perhaps a little more prompt.

DISCUSSION.

Mr. WEST congratulated Mr. Mollison on the result which the disease and the surgeon between them had achieved. He confessed that, in some ways, it was to him a most astonishing case. There was a canal fistula; a probe was introduced through the canal, in its anterior part, so that the probe went into the ampulla, and probably into the vestibule. The fistula was enlarged by the burring, and in the end the hearing of the patient was most unusually good after the radical mastoid operation, both for speech and other forms of sound. He hesitated very much about putting probes into fistulae in canals. Assuming the labyrinth was not involved, it seemed to him that in a canal fistula one was dealing either with a labyrinth in which the periosteal lining of the canal was intact, and one would risk its rupture and acute infection of the labyrinth by the probe, or in which, at all events, the labyrinthitis had been so limited as to involve merely a small section of the canal. He did not know the practice of other members, but when he met with canal fistula and an active labyrinth, he merely scraped the softened edges of the fistula with a small spoon, and in a general way treated it with the utmost respect. But after hearing about this case, he might feel more bold in his exploration in future. He would be glad to hear if any members could trace any ill-effects to the use of the probe when the operation was not extended to the complete drainage of the labyrinth.

Dr. DUNDAS GRANT suggested that the scraping away of the epithelial membrane lining the cavity was a proceeding about which there was room for more than one opinion. In his earlier experiences he had a large number of cases in which he preserved this epithelial lining after operating; and he had seen cases in which this beautiful pearly lining was left after the spontaneous extrusion of cholesteatoma, such as Mr. Mollison described in this case. The healing in those cases was particularly rapid and good. His experience might have been exceptional, but this had been the experience of others also. He did not doubt that in this case, which could not be called Nature's operation, the result was very fine. He did not think the lining should always be taken away. The reason he had not seen so many favourable cases within late years was probably that cases had not been allowed to go on so long, as the production of such a lining required a long time.

Mr. JENKINS asked if Mr. Mollison actually did pass a probe into the canal. He said a small probe could be passed. If Mr. Mollison did pass it into the canal, it was difficult to account for some of the subsequent symptoms.

Mr. SYDNEY SCOTT said he considered there were two chief items of interest: First, that the cholesteatoma "performed" the radical mastoid operation. He was reminded of a similar case which Mr. Nixon Biggs showed the Section a few months ago, and of two other cases which he had seen in his own practice. The other interesting feature was the question of the labyrinth. With regard to probing a labyrinthine fistula and its effects on hearing, he would like to remind members of a case which was shown before the Section some months ago in which a probe was passed, not into the external canal, but through a large fistula of the superior canal into the vestibule, and yet the patient's hearing was not disturbed by the procedure. Nevertheless he would not advocate the use of the probe as a routine examination.

The PRESIDENT said that one point which struck him as of interest and as curious was the short duration of the case. The patient had suffered from otorrhœa for eight months, and this seemed a very short time for cholesteatoma to have done so much damage. He thought there must have been some semi-quiet condition going on for years. With regard to passing a probe into or through a fistula in the external canal, he had always avoided doing this; but at the same time he could not see why, even if it were done, the hearing should not be preserved. There was such a thing as a circumscribed labyrinthitis, and if adhesions formed there was no reason why the integrity of the cochlea should not be preserved.

Mr. MOLLISON, in reply, said he explored the fistula with a fine Jansen's probe; he did in every case what he did in this, so as to make quite certain that the fistula went through the bone. He had never seen disaster follow from the procedure, although he had seen about eight cases during the last year. He had seen hearing preserved after opening the fistula in the canal in two or three cases. With regard to the suggestion that the discharge had been going on more than eight months, he thought that was very probable, for the statement as to the duration was on the patient's word alone.

Case of Mastoid Cyst after Operation.

By RICHARD LAKE, F.R.C.S.

CHILD, aged 12, had acute right mastoiditis in infancy, which was operated on. She recovered, with loss of power in the facial muscles on that side. She then developed Pott's disease, and later a chronic left otorrhœa began to give trouble. Origin of otorrhœa uncertain. Mastoid operation; eventual cure. There was now a discharging sinus in upper part of antro-meato-tympanic cavity, which was originally a thin-walled cyst. The contents were a thin, grumous, brown fluid; this comes away now to some extent.

DISCUSSION.

Dr. LOGAN TURNER asked if Mr. Lake was sure there was a cyst, and if it was not, or might not be, a diseased pocket, in old mastoid cavity.

The PRESIDENT said the ætiology was an interesting point, and he would like to know if Mr. Lake did not consider it a tuberculous lesion?

Mr. LAKE, in reply, said it was a cyst when he first examined it, as he put a knife into it and obtained from it grumous fluid. He did not doubt that the lesion was a low form of tuberculosis. The history of the patient was a tuberculous one.

Case of ? Exostosis of the Promontory.

By RICHARD LAKE, F.R.C.S.

PATIENT with a dry ear, the site of a discharge of many years. The promontory shows a small, almost spherical knob.

The PRESIDENT said he thought the spherical knob looked like the head of the stapes, somewhat dislocated downwards.

Patent Eustachian Tube after Mastoidectomy in a Girl.

By E. A. PETERS, M.D.

THE operation was performed on September 15. Skin-grafting was done a fortnight later, and it healed very successfully, with the exception of a small moist spot at the upper part of the ear. Apparently that was not directly over the opening of the Eustachian orifice, but it led down to it, as lotion passed into the throat. There was a thickened pseudo-membranous ligament across the lower part of the ear, and at present a probe did not reach beyond, so there was no pocket. Opinions were invited as to whether it was advisable to close this further, or to leave it open. At the time of the operation a curette was introduced into the mouth of the tube, which was gently curetted.

DISCUSSION.

Dr. LOGAN TURNER said the case ventilated a very important matter in connexion with mastoid operations, for in his experience there was nothing more difficult than to get a permanent and complete closure of the Eustachian

tube; one might use sharp spoons and burrs, and recently he had been using the Yankauer curettes, which brought about a more thorough curettage. But even with this the operation did not turn out satisfactorily. He had no doubt that it was necessary to close the Eustachian tube in many of these cases. It was only necessary to watch the mucoid discharge which was seen in the tympanic cavity after mastoid operations to enable one to realize that the discharge was coming from the nasopharynx and Eustachian tube.

Mr. LAKE agreed with Dr. Logan Turner as to the extreme difficulty of closing up the Eustachian tube in such a case. He did not see how one could do so by curetting. Apparently this was the wrong way to attempt it, as the tube had a solid wall. The case would be different if there were soft walls to the Eustachian tube, for then by curetting away the mucous membrane one would find that the cicatricial tissue would form a stricture, and probably entirely close up the orifice. What was required was to give a redundancy of tissue. If one were not working at an awkward angle, it would be reasonable to try to reflect the mucous membrane round the Eustachian tube and tuck it in. But it was beyond the dexterity of his fingers to accomplish this.

Dr. DUNDAS GRANT said it was most important to attend to the healthy condition of the nasopharynx. Very often with patency of the Eustachian tube there was an excess of mucus in the middle ear after the radical mastoid operation on the occurrence of a catarrh. He did not think that the small amount of moisture there did any great harm; it only meant that the nasopharynx was in an unhealthy condition.

The PRESIDENT said he was an advocate of closure of the Eustachian tube, but he had found difficulty in accomplishing it. He had found the best thing was to preserve, if possible, a small portion of the tympanic membrane, and fold it back over the mouth of the Eustachian tube. This was far better than curetting, and made a more durable cicatrix.

Dr. PETERS, in reply, said it had occurred to him as feasible to inject paraffin at the time of the mastoidectomy. He wondered if this had been tried.

Malignant Tumour of the Nasopharynx associated with Deafness, Neuralgia, and Weakness of the Levator Palati.

By HERBERT TILLEY, F.R.C.S.

S. H. B., MALE, aged 41, consulted me on April 29, 1909, for deafness in right ear of six weeks' duration. There were no pain, discharge, or tinnitus. Ordinary tests revealed middle-ear deafness and the presence of fluid in the tympanum. Paracentesis and evacuation

of clear serous fluid was followed by immediate restoration of hearing, which became duller the same evening, but on the whole remained better for "some months."

Seen again on April 10, 1910. Hearing very defective; examination proved that fluid was present in tympanum, and membrane was punctured again, and from now onwards there was a certain amount of discharge, which was small in amount and was treated by the instillation of "spirit drops." The hearing did not improve.

Early in January, 1911, he noticed a "small lump" in upper part of right neck, and consulted his doctor, who thought the swelling was a tuberculous gland because of strong tuberculous history in members of family. Neither the doctor nor a consulting physician could find any signs of tubercle in the lungs, but in view of tuberculous history injections of tuberculin were given, and the second injection was followed by an evening pyrexia (101° to 102° F.), which lasted for six weeks, and only ceased when open-air treatment was commenced. Only the two injections were given.

About six weeks after the second injection of tuberculin severe neuralgia commenced, chiefly affecting the right temporal region and behind the ear over the lower mastoid region. It lasted severely for six weeks and rather shifted to the region over the right lower jaw and into the "glandular swelling." When the pain was severe there was a feeling of numbness and stiffness over the mandibular region. Associated with the neuralgia was a difficulty in opening the mouth, so that he found it easier to take soft food with a "spoon or the blade of a knife."

Some four to five weeks ago he went to a general hospital with a view to removal of the gland, when an examination of the nasopharynx revealed a tumour in the right side of this region; a small portion was removed for examination and was said to be "sarcomatous." Since this removal the patient says he can open the mouth wider—a fact I can confirm, because he lunched with me yesterday and had no difficulty with ordinary soft food. The neuralgia is much better than it was, possibly because by taking aspirin, which quickly relieves the pain, the patient does not allow it to become severe.

Since April 10, 1910, till yesterday (November 16, 1911), I had not examined the patient, when I found the following conditions: Slight loss of nasal resonance in voice; marked deafness in right ear; slight discharge from right meatus, with perforation in anterior inferior quadrant of tympanic membrane; tests proved deafness to be of middle-ear origin; a hard swelling behind the ascending ramus of

jaw; defective mobility of right side of soft palate; the lower edge of a nasopharyngeal growth seen behind and below the right free edge of soft palate, which could be seen in fuller extent by posterior rhinoscopy. Digital examination revealed a definite, smooth growth occupying the right side of the nasopharynx, and obscuring the Eustachian orifice and other anatomical features. This examination was difficult, because of the difficulty of opening the mouth widely. The anæsthesia over the right lower jaw is not very marked. This case is almost identical with the one which I saw with Dr. Edward Law and reported by him to this Section,¹ and also with those which form the subject of Mr. Trotter's paper in the *British Medical Journal*, October 28, 1911, "On Certain Clinically Obscure Malignant Tumours of the Nasopharyngeal Wall."² In all of them is to be noted that curious and almost diagnostic combination of early symptoms—viz., deafness, neuralgia of the second division of the fifth nerve, and impaired mobility of the levator palati muscle. The most common growth producing these symptoms is endothelioma.

In this case, which is now in an advanced stage, operation is out of the question, and we propose to try the application, internally and externally, of radium.

Note.—The early history is given in some detail, because of the prominence which was given to the tuberculous family history.

DISCUSSION.

Mr. MARK HOVELL suggested that Coley's fluid should be tried, as he had seen beneficial results from that treatment.

Dr. DUNDAS GRANT said that at the present time he had a case under observation somewhat similar, but fortunately he got it in an early stage. The patient came to him four weeks ago on account of hæmorrhage, sometimes from his nose and sometimes from his throat. He looked in the usual spots, and saw nothing to explain the hæmorrhage until he examined the nasopharynx, and found what seemed to be a mass of adenoids. On the next visit deafness had developed, and he removed a small portion of the growth for examination. It turned out to be a somewhat indefinite epithelial growth. By means of the post-rhinal mirror he saw that it was chiefly confined to the left side. In the nasopharynx it appeared exactly like adenoids, but it was somewhat more papillated, and hard to the touch. One could feel very deeply over the styloid process a gland which was tender on pressure, and the case would shortly be operated upon by Mr. Wilfred Trotter.

¹ Vide *Proceedings*, 1910, iii, p. 28; 1911, iv, p. 67.

² *Brit. Med. Journ.*, 1911, ii, p. 1057.

Dr. FITZGERALD POWELL asked if Mr. Tilley could tell him what was the site of origin of this growth, if in the antrum, nose, or the post-nasal space. The case was a very bad one, but he thought Mr. Tilley had operated on cases as bad, and he himself had certainly got prolongation of life in similar cases on which he had operated: and the patient was kept going for some time by repeated operations when recurrence took place; besides, the patient was much more comfortable than if the growth was allowed to go on without operation. The man was young, and he did not think he should be left to the doubtful benefit of radium in such an inaccessible part.

Dr. DAN MCKENZIE said that he remembered that some years ago Mr. Stuart-Low had, at the Central London Throat and Ear Hospital, a case very similar to this in regard to the ear symptoms, but not showing the appearance of tuberculosis. The patient was an old man who had developed a discharge from his ear, and it was in the routine examination of the case that the discovery of a tumour in the nasopharynx was made. A small portion was removed for examination and was found to be endothelioma. A curious coincidence was that the following week, in the out-patient department, another old man came to him with a similar history—namely, that of an ear discharge of recent origin. The man was deaf, and had some pain in his ear. On examining him with the post-nasal mirror a growth was seen, and this also turned out to be an endothelioma of the nasopharynx. In neither case was the growth removable, and the patients disappeared from observation.

The PRESIDENT said there was a very important otological lesson to be derived from Mr. Tilley's communication, which was brought forcibly home to him a few years ago. This was that when there were frequently recurring attacks of sero-mucous catarrh in one or both ears, most minute attention should be paid to the nasopharynx. One was apt to put it down to cold, to say the person had got a cold again, and the result was that an exhaustive examination of the nasopharynx was not made. What brought this to his mind was that a good many years ago he was consulted by a lady, who for some months had very severe attacks of catarrh in one ear. On her coming to him again, after an interval of several months, he found there was some definite infiltration in the nasopharyngeal mucous membrane. It turned out to be a case of carcinoma. Ever since that date, whenever the patient was beyond middle age, he dismissed from his mind the question of cold, and looked out for something worse. With regard to treatment, he would not take the absolutely pessimistic view which Mr. Tilley did, but would be inclined to perform a temporary resection of the upper jaw, and see if the growth could not be removed. He had seen, and successfully operated upon, cases which at first sight seemed to be quite inoperable. Now and then there had been a case in which by doing a fairly formidable operation—either excision of one half of the upper jaw or temporary resection of the upper jaw—the growth had been successfully removed. And although he could not give a

case in which recurrence had not taken place, he agreed with Dr. FitzGerald Powell that the end of such a patient was easier than if no operation had been carried out. He suggested that perhaps Mr. Tilley would reconsider the question of operation.

Mr. TILLEY, in reply, said that a very able and brilliant operator had seen the patient and declined to operate; his opinion was that no permanent good would come of it. When one saw the jaw swung out, and the amount of infiltration which had taken place towards the base of the skull and into the neck, one realized why most of the cases were so hopeless. The patient was a young man, and was anxious to have anything done which would be of benefit. He would be pleased to inform him of the opinions which had been expressed at the meeting, but his own opinion was that it was a bad case, because it infiltrated the whole lateral wall of the post-nasal space so that it could be felt in the thickness of the sub-epithelial tissues about as far as the middle line. To get such a growth out successfully would be a very difficult task. There was no growth in the nasal sinuses; it was a deeply penetrating infiltrating growth starting in the nasopharynx below the Eustachian tube, and extending externally into the upper part of the neck. He was much obliged to Mr. Hovell for his suggestion regarding Coley's fluid. If an operation were decided on and the growth recurred, he would resort to Coley's fluid or radium, or any other agent from which relief might be obtained. If radium was selected in place of an operation a powerful application would be made externally as well as to the growth in the nasopharynx.

Notes of a Case of Brain Tumour (?) associated with Chronic Suppurative Otitis Media.

By D. LINDLEY SEWELL, B.S.

PATIENT, J. F., aged 31, male, referred to me on September 8, 1911, by Dr. H. H. McNabb, whom he consulted on account of total blindness of three days' duration. History: That one month previously severe vomiting and dizziness occurred, lasting five days, both recurring three weeks later, occipital headache severe and continuous—loss of weight about 14 lbs. Right ear had discharged for eighteen years—on examination pus foul, with pale granulations growing from the middle ear; acoumeter, 5 in.; bone conduction (*C* 256), normal; Rinné negative; Weber lateralized to right; no "fistel-symptom"; active response to caloric test; no tenderness over mastoid region, but right occipital region tender on percussion. No nystagmus. No paralysis of ocular

muscles; pupils dilated; react sluggishly to light; intense optic neuritis both sides. Head retracted; neck stiff. Romberg's test, swayed to right side; on walking stumbled to right side. Knee-jerks absent left, present right side. Babinski left (?). Kernig's sign present right and left. Dysdiadokokinesia marked both arms. Pulse, 66; temperature, 99.4° F. Operation the same evening—usual post-aural procedure. No definite carious track leading intracranially found. Posterior fossa exposed between sinus and labyrinth, but no pus discovered on exploring; middle fossa then exposed, and temporal lobe explored with negative result; great escape of cerebrospinal fluid; dura then exposed over wider area and incised. Previously to exploring the brain, repeated attempts to obtain cerebrospinal fluid by lumbar puncture failed.

Following operation complete relief to headache, and no further vomiting took place. For the first three days there was perception of light, complete blindness then recurring. Cerebrospinal fluid continued to escape freely, and a large hernia of the temporo-sphenoidal lobe formed. Patient stayed in hospital for four weeks, his pulse remaining about 66, and his temperature running from 98.4° F. to 99° F., then taken home, and at the time of writing is still living.

While in hospital he was seen by Mr. P. R. Wrigley and Mr. Garnett Wright, who advised against any further operative procedure.

A probable diagnosis of cerebellar abscess was made on first seeing the patient, the presence of a suppurative otitis media making this a possibility. It seems evident that the diagnosis was wrong, and that some form of brain tumour is the lesion.

Otological Section.

January 19, 1912.

Dr. W. MILLIGAN, President of the Section, in the Chair.

Factors which conduce to Success in the Treatment of Otogenic Brain Abscess.

Addresses Introductory to a Discussion on the Subject.

(I) By Sir VICTOR HORSLEY, F.R.C.S., F.R.S.

As regards "the factors conducing to success" in these cases, I take it that the chief one is the early detection of the abscess and its correct localization. But there is a point associated with the pathological process itself on which I should like to hear the opinions of members of the Section from the point of view of its importance. I have here two of the last patients on whom I have operated, and in each of them it is quite obvious that the process was continuous throughout, from the first infection of the ear to the development of the abscess. I wish to suggest that very often a case of otitis media, especially if one has treated it by the mastoid operation, is regarded as being well when it is not really well, and I would like to ask the Section whether any "mastoid" case not dry ought really to be considered well. The child here is a very good instance in point, because the whole process was very acute. The mastoid operation was performed in Wales and the child appeared to be quite well; nevertheless it must have had symptoms at that time, symptoms which I shall refer to directly, for when she came to the hospital the condition was very obvious. Under these circumstances, I suggest that there are two points of view from which

we should watch these chronic otitic cases: the bacteriological point of view and the neurological. With regard to the first, naturally, by blood counts and opsonic tests we could have a clinical record from the time of infection, by means of inspection and examination, at regular intervals. In that way we could, in all probability, anticipate the discovery of abscess or the outburst of meningitis.

Now with regard to the neurological part. I draw attention to the fact that, many years ago, Sir Russell Reynolds pointed out that in cases of otitis media chronica the reflexes were not normal; that, in fact, the reflexes on the opposite side of the body were altered. And almost the very first case of mastoid operation which was ever referred to me was a case of this kind, sent by Sir Russell Reynolds. So this is not by any means a new subject. I propose, therefore, that these cases should not only be constantly re-examined bacteriologically, but they should also constantly be re-examined neurologically, and the reflexes will be found altered on the opposite side in most cases. I ask those who have special experience of the enormous amount of material in our schools as to what they have found on this subject, because I am sure attention must have been directed to it. I pass by the well-recognized necessity of constantly examining the fundus oculi—I only wanted to emphasize the fact that, primarily, we should examine these patients neurologically. May I put in a word here for more frequent bone operation, because all the records of abscess in the adult go to show that it is due to prolonged infection of the bone. If we have prolonged infection of the bone it means we have not been sufficiently industrious in cutting away the diseased tissues.

So much for preliminary conditions. I now come to early detection of cerebral disease—excluding, of course, sinus thrombosis. What is the difficulty which presents itself to us in the vast majority of cases? The fundamental difficulty is the distinction between abscess and meningitis. Differentiation is often not clear, because naturally the two things are not infrequently combined. But upon what, especially, can one rely for the early detection of the one or other condition, and for its subsequent accurate localization? I shall only detain the Section by running over four or five cardinal symptoms, and I shall ask for the experience of members on those points.

It is a matter of belief with me that by the pulse alone we can distinguish between these two conditions. I believe that in meningitis the pulse-rate and pulse-force will always exhibit an irregularity which is not met with in abscess, unless the abscess is highly complicated.

Further, then, in contradistinction to the irregular and relatively small pulse of a case of meningitis, we have the regular and full pulse of the abscess case. And this, I believe again, is not purely a matter of pressure; the abscess pulse is not a mere compression pulse, but it is partly due to the difference in the affection of the cardiac nervous apparatus. In abscess you have a localized lesion which, for instance, often does not (like the meningitic process) directly affect the roots of the vagus.

Now with regard to temperature. Here I want to delay a little longer, because the question of the temperature has special significance in the differential diagnosis of these two conditions. I do not think anyone has yet described a case of meningitis simulating abscess with a low temperature. And then, on the other hand, although it is becoming more gradually recognized and is to be found in the text-books, I am sure that the point first taught by Sir Samuel Wilks—that of depression of temperature—is not accurately appreciated in proportion to its significance. Nor, indeed, is the frequency of it fully recognized in practice, although, as I have said, it is now found to some extent in the text-books. In the first place, with regard to this question of the lowering of the temperature, and to what I was saying just now as to the continuity of the process, Professor Oppenheim suggested that we only get a lowered temperature as a characteristic symptom of abscess of the brain simply because we have overlooked the first stage of high temperature. I am not at all satisfied on that point, because in a traumatic case I have seen suppuration develop with a low temperature where there had been no previous rise. I think we have yet to explain why Wilks's symptom exists. But my point at the moment is simply to urge that it is always present, and that it is an essential characteristic. Both the cases I show here this afternoon have exhibited it; and Sir William Macewen shows that where there is no absolute abnormality (and we do not know the normal temperature of these individuals since we have no opportunity of testing it beforehand) the temperature is normal.

So much for the actual degree of the temperature. Now a word as to the use of the temperature as a means of localization. When an otogenic abscess is in the cerebellum or in the temporal lobe the text-books allude to the lowering of temperature, but not to another clinical feature with regard to its use in diagnosis; I have drawn attention to this for many years, but it has not been brought into the text-books to any degree, though it comes in with special value here, because

in all cases of cerebral abscess the real difficulty is to express a positive opinion as to whether the abscess is single or multiple. The heat-regulating centres are in the Rolandic area, probably in the precentral gyrus, and if a lesion is situated in the coronal plane through the Rolandic area, the temperature rises on the opposite of the body. In such a case there is a depression in the heat-controlling centre, but, provided you are dealing with a lesion posterior to that plane, there will be no rise of temperature on the opposite side of the body. And so also if the lesion is anterior to that plane, that is to say, the frontal mass or the temporal region, again there will be no rise of temperature on the opposite side. So also if there is a lesion in the cerebellum there is no rise of temperature on the opposite side of the body, nor even, as far as I have seen, on the ipso-lateral side. Therefore it is not sufficient to take the temperature to see whether it is high or low; we take the temperature from the point of view of accuracy of localization, to help to decide further whether an otogenic abscess is single or multiple. In a multiple case the second abscess is usually in the parietal region, where it also almost invariably occurs as a complication of chest disease.

So much for the temperature. Now I pass quickly to the next symptom, and that is the question of motor paralysis or motor loss. Of course it has long been known that, inasmuch as we have the base of the brain resting on the absolutely rigid skull, and the pus collects, for instance, in the temporal lobe—I am speaking of cerebral abscess—the pressure rises vertically, and therefore you have a graded hemiplegia—the face being most involved, then the arm, then the trunk, and lastly, the leg. The little girl sitting here is a case of that kind. Her hemiplegia has now practically disappeared. She had an enormous abscess in the right temporal lobe, and she had left hemiplegia of that very striking type. But I only raise this point now in order to re-affirm this essential point in diagnosis, and to draw attention to another. It is now generally recognized that of the two Rolandic gyri the posterior is more sensory in function than the anterior. And I have previously drawn attention to the fact that when you have a pressure lesion of one hemisphere, if that pressure tells on the Rolandic area posterior to the coronal plane through the Rolandic fissure, then, although the motor paresis may be almost unnoticeable, there will be detectable a delicate loss of the sense of localization of position—i.e., the point touched—which sense I suggested should be called *topognosis*. In otogenic abscess in the temporal lobe the pressure comes first almost on the sensory motor area before pressing on the pyramidal fibres. But the pyramidal fibres

take an oblique course, so as to get to the thalamus. Therefore, in these cases, at a time when they may yet be considered to be practically well, I think that if a minuter examination of them were made neurologically—both from the motor standpoint and topognostic sensory standpoint—we should discover changes which might make us suspect the development of abscess earlier, and by operating earlier should have better success.

Consideration of the mechanical conditions in the hemisphere brings me at once to the question of the reflexes. I simply want to point out here that we have absolute evidence at our disposal on the differential diagnosis, because in meningitis the superficial reflexes soon disappear and are bilaterally affected; whereas in abscess they are unilaterally affected, and it is a long time before they disappear. Changes in the abdominal reflexes precede, and continue far longer than, the changes in the knee-jerk; and thus the importance of investigating the abdominal reflexes is far greater than that of investigating the knee-jerk.

Lastly, I want to refer to the question of optic neuritis. This is, of course, a very large subject in connexion with otitis media, but I hope I shall be able to say, what I want to particularly, in a few minutes, again purely on the question of localization. The constant examination of the fundus oculi shows in these cases that the vascular changes do precede the neuritic changes. They show, in my experience, that you can detect an over-filling of the retinal veins on the ipsolateral side. But as regards the difference between meningitis and abscess, we should expect fundamentally that there would be a difference between the conditions, because in meningitis we have universal pressure on both halves of the brain. Therefore we ought to have a perfectly bilateral neuritic change developed, and I suggest that that is the case. I suggest also, from the examination of a large number of cases, that the meningitic cases show a highly oedematous, greatly swollen disk in contrast to the very modestly swollen disk in the case of abscess. The appearance of the neuritis when it is developed, therefore, is different in the two conditions. As regards this point also, I would ask the experience of the Section as to the well-known fact of optic neuritis accompanying the petrous bone disease met with in children. I believe that sufficient attention has not yet been given to its development. I wish to allude to a case which I saw with Mr. Sydney Scott some time ago, in which the development of the neuritis was so singularly characteristically local—that is to say, the

child showed the commencement of neuritis in the upper part of one disk only—and that was the side of the affected ear, as you would suppose. And on that point alone decision could be taken as to whether further active operative measures should be pursued in regard to the case. (Such treatment was successfully carried out by Mr. Sydney Scott.)

Now we come to the condition of things in abscess. The patient here, the adult, is a typical case in point. He was sent to me by Dr. Grindley, of Olney, with a history of double otitis; and when he came to my room, at my house, he was obviously extremely ill. I could not prove that he had cerebellar abscess, but I sent him immediately into the hospital for inspection. He was there almost a month under our observation, in which I had the assistance of Mr. Scott. I saw him on January 1, 1910, and he was rather worse constitutionally. All symptoms pointed towards the left cerebellar lobe, but the decisive point was that he had commencing neuritis in the upper border of the left disk, and nothing at all in the right. I immediately took him into the theatre, opened the left lateral lobe of the cerebellum at *that* point, and there was an abscess which subsequently healed well. That was two years ago. On this question of ipso-laterality, of course, my colleague, Mr. Paton, does not see eye to eye with me; and it is rather amusing that on looking over the old notes I find he saw this particular case a few days afterwards and described the disks as apparently similar. My physician-colleague, Dr. James Taylor, under whose care also the man was, re-examined him on several occasions, and on each took the view that I did—that the neuritis was worse in the left eye. This little girl also exhibits precisely the same point. Her neuritis has totally disappeared, and therefore there is nothing for you to see. I have had her fields taken by Mr. Prentice, because in these cases of doubt you may trace the subsequent changes in the optic nerve; and I will show you her fields for different colours. Her abscess was in the right temporal lobe, and for white light she has a marked loss in the right field compared with the left. The next slide shows her field for red, and you see the same thing very markedly. The next is for blue. For green it is exactly the reverse, since the field is rather better in the right eye than in the left. I think that reversal is another instance of the same condition which has been shown by Cushing to exist in cerebral tumour.

I have said nothing on the question of technique, because, to my mind, there is nothing specially to be said upon that; it is only a

question of adequate drainage and vaccination, and that is the way in which all my cases have been treated of recent years. With regard to drainage, it is often mechanically a difficult matter. I have always, in recent years, employed concentric tubes, so that, as far as possible, there has never been a tube removed from the wound until the final granulation occurs.

(II) By C. E. WEST, F.R.C.S.

When the subject of this discussion was proposed to the Council, my enthusiasm for it was misinterpreted, and my eagerness to learn was taken to be capacity to impart knowledge. So I became a reluctant opener to-day. In mere fact, my personal experience has been too small to be of much value, and I hope to carry away far more from others than there is any prospect of my being able to give to them.

In the pathological anatomy of temporo-sphenoidal and cerebellar abscesses there are points of extreme importance which influence the patient's prospects of recovery very markedly. These concern the meninges, the ventricular system, and the vital parts of the brain. In temporo-sphenoidal abscess the area of infective entrance above the tegmen is usually adherent to the dura mater, and the leptomeninges are soldered together at this point; the risk of meningitis from the spread of infection in this region is consequently a small one except through operative disturbances. It is, I think, rare to find more than a plastic meningitis surrounding the firmly adherent stalk of the infected part of the brain. I doubt whether abscesses ever "burst" into the meninges at this point. On the other hand, they may drain themselves partially and intermittently through the tegmen tympani. In the lateral ventricle—its descending horn—we have, on the other hand, a circumstance of extreme geographical importance in temporo-sphenoidal abscess. Abscesses of even moderate size come into dangerously close relationship with this cavity on their inner aspect, while the larger ones necessarily abut directly against its wall. Even when as much as half an inch of brain substance intervenes, the ventricle is often somewhat distended with cloudy fluid; in the larger abscesses the wall of separation may be thinned out to a mere veil of ependyma. While the effusion of fluid in the ventricle may offer some measure of support to the wall of the abscess, it at the same time makes

adhesion and obliteration of the cavity impossible. As a consequence, not only does infection of the ventricles often take place by the passage of organisms through some thickness of brain tissue, but it is not rare for a true burst to take place into the ventricle, with the production of a very typical and very certainly fatal set of symptoms. When this happens, the whole of the ventricular system seems to become rapidly permeated by infection, and this may then escape through the connexions of the ventricular system with the subarachnoid space, with the production of a terminal meningitis. The slower entrance of organisms into the ventricle through the substance of a septum intervening between the abscess and the descending horn may, on the other hand, allow of a certain amount of localization, and I have seen the descending horn full of pus and the surrounding brain diffuent, while the body of the ventricle contained fluid scarcely turbid and that of the opposite side was apparently normal. The danger attending the introduction of drainage-tubes too deeply into an abscess cavity and of thus penetrating or injuring a thin wall of separation from the cavity of the descending cornu is too obvious to be worth more than a passing mention. In temporo-sphenoidal abscess the vital parts of the brain, the great organic centres, are remote, and are largely shielded from immediate pressure by the intervention of the tentorium, while the upper levels concerned in consciousness and mental activity are directly affected. It is very remarkable how even the most profound coma may be recovered from after the relief of pressure in temporo-sphenoidal cases, and with what vigour respiration and circulation may be continued long after consciousness has gone. So far as I have been able to see, the loss of even large portions of the temporo-sphenoidal lobe, both cortex and white matter, makes very little difference to the patient intellectually or motorially; but my experience in this respect has been confined to hospital patients. It is possible that with the finer mental processes of an educated person the loss would be more apparent.

In cerebellar abscesses the position with regard to the meninges is modified by the deep penetration of the fissures into the substance of the cerebellum, so that in section the appearance of the brain is almost racemose, and on the other hand by the fact that the subarachnoid space does not penetrate within the sulci, the pia mater bridging them. It is often difficult or impossible to say how far an abscess is truly within the cerebellum and how far it is interlamellar, lying between and separating the softened cerebellar folia. Adhesion

takes place as a rule at the point of entrance of infection through the bone or sinus, but secondary infection of the meninges is far more common than in temporo-sphenoidal abscess, and this infection often spreads over both upper and lower surfaces of the cerebellum, leading in the latter case to a general basal infection. Cerebellar abscesses generally lie at some distance from the fourth ventricle, and become fatal from other causes before they have extended sufficiently to imperil the direct infection of the ventricles. The ventricular system is involved in different fashion, however. Direct pressure may close the apertures by which the communication between the fourth ventricle and the subarachnoid space is secured, or these openings may be sealed by a plastic meningitis in cases of mild infection of the meninges in the neighbourhood of the posterior surface of the petrous; in either case the result is an internal hydrocephalus, and death from pressure generally ensues. The primary vital centres in the bulb, especially the respiratory, are exposed to direct pressure in cerebellar abscess, so that vital functions may be endangered while consciousness is comparatively slightly affected. Finally, in severe secondary meningitis the fourth ventricle may be infected through the lateral apertures of Key and Retzius, or the mesial foramen of Majendie.

The cerebellar abscess which is secondary to lateral sinus thrombosis lies at the outer pole of the lateral lobe, and is remote both from the apertures of communication of the fourth ventricle with the subarachnoid space and from the vital centres in the floor of the ventricle. It is easily accessible and easily drained. In so far as the abscess only is concerned, its prognosis is better than that which is secondary to labyrinth infection, which, lying more deeply, under the anterior surface of the lateral lobe, is both more difficult of access and drainage, and is more apt to cause dangerous pressure on the centres of respiration and of the heart's action. While even severe compression of upper centres may be recovered from, there seems to be a point, often short of temporary suspension of function, at which the vital centres, especially that of respiration, are unable to recover, and the patient dies in spite of the effective relief of pressure.

If we strike a sort of balance, the geographical features will be in favour of the temporo-sphenoidal lobe as regards the likelihood of meningitis and interference with vital centres, adverse in respect of the danger of ventricular infection; while they favour recovery in cerebellar cases as regards ventricular infection, but are adverse in respect of pressure on vital centres and of meningitis.

Geography affects also the prospects of effective relief by operation, and here the balance is undoubtedly in favour of the temporo-sphenoidal lobe, with its advantages of easier access, wider possibilities of exposure, and better drainage position.

Brain abscesses vary widely in the degree of their limitation, and this is proportional in the main to the acuteness or chronicity of the condition. There may, on the one hand, be a purulent area in the midst of acutely inflamed or necrotic brain substance which spreads far beyond the neighbourhood of the formation of pus, and, on the other, an abscess may be sharply limited by a capsule from surrounding almost normal brain. In the majority of otitic abscesses, limitation is incomplete, there is no definite abscess wall, and the surrounding brain is softened and infected. An extreme condition in either direction is unfavourable; on the one hand, it is impossible to drain a widely infected mass of brain without destroying its structure, and even under the most ruthless treatment the problem is one of extreme difficulty; on the other, a very thick and firm abscess wall makes sound and permanent healing very difficult to attain, the cavity never becoming really obliterated, even after prolonged drainage. The very chronic abscesses probably arise in two ways, either as a chronic condition from the first, as in tuberculous abscesses and in attenuated pyogenic infections, or as the result of localization of pus formation in an infected area, the resolution of the surrounding inflammation, and the dying out of active organisms in the pus. The abscess then practically becomes a cystic tumour with a gradually thickening wall.

Our knowledge of the bacteriology of brain abscess is not in a very satisfactory position. In the ordinary otitic abscess, with direct infection by continuity, occurring nearly always in chronic middle-ear suppurations, infection is from the first highly mixed, and the pus has substantially the same bacterial character as that from the ear. Pathogenic cocci are often difficult to find in films, and impossible to isolate in culture. Gram-negative bacilli of the coli group, putrefactive organisms of the proteus group, pyocyanus and fluorescens, often crowd the field and overgrow the plate pitilessly. I have seen long branching filaments of a streptothrix, and once found the film full of a coarse spirochæte like *Spirochæta buccalis*, associated with Gram-negative bacilli. Rarely the influenza bacillus is recovered; this was the case with a recent cerebellar abscess of mine. In many of the more chronic abscesses, and even in some acute ones, nothing is grown by the ordinary methods. Probably if anaërobic cultures were made

the report of sterility would be much rarer than it is. The very densely capsuled abscesses seem to be generally pneumococcal, and are in many cases pyæmic if their situation is a guide. This unsatisfactory position with regard to the infective agent reacts unfavourably on treatment, as it blocks the way to any intelligent application of sera or vaccines where the infection is spreading. A few abscesses are due to *Staphylococcus aureus*, and it is worth remark that this organism may apparently act as a gas-producer in the brain.

I have tried to put forward a few points which may offer a scaffolding for the discussion of the influence of morbid anatomy in cases of brain abscesses. Under the heading of treatment I shall draw on such experience as I have for a few details which seem to me important. In temporo-sphenoidal abscess I always use the single route from below for drainage. It has the great advantage of following the track of infection and of opening through the area of adhesion of the meninges, while pus is reached through the minimum thickness of brain tissue. A counter-opening seems to me to endanger the meninges, and necessarily to lead to the infection of fresh brain substance. Except in cases of large and well-defined abscesses, I very much doubt whether any increased efficiency of drainage is obtained by the second opening. In cerebellar abscess, except those associated with lateral sinus thrombosis, the route to the inner side of the sinus seems to me that of choice whenever there is reasonable space to be obtained. In some cases, however, the anatomical difficulties are extreme. It is hardly necessary here to condemn the use of the trephine in otitic abscess of the cerebellum.

I attach great importance to doing as little damage to brain tissue as possible, and particularly to avoiding laceration of the limits of the abscess. I always use an expanding trocar to explore the brain. Once pus is found, the instrument is not moved from its position until the tube has been introduced between its limbs. It is very easy, otherwise, to fail altogether to get a tube into the site of suppuration where there is a small abscess in the midst of an area of infected and softened brain.

Where the abscess is well defined, I think it will be generally admitted that tubes form a satisfactory means of drainage. I use rubber tube of good size, up to the thickness of the little finger, or a pair of tubes of smaller size stitched together with a silkworm-gut suture. If the tube is stitched to the edge of the dura mater, or to some other convenient point, and it is of good size, it will not be

pressed out by the brain. I have abandoned all lateral holes in tubes. They become blocked immediately, and large plugs of brain are torn away each time the tube is rotated or removed, exposing fresh surfaces to infection. In any case I fancy that most of the drainage secured by a tube takes place along its surface. The problem of drainage of areas of diffuse infection seems to me one of extreme difficulty. Tubes I admit to be ineffective, but I have no fondness for gauze, which has been very unsatisfactory in my hands, especially as prolonged drainage by its means is practically impossible. In bad cases I believe the method used in a case I once mentioned to the Section is the only one which offers any hope, that is, the bold removal of a wide area of bone and dura mater, and then of the overlying cortex, so that a large amount of the infected brain is exposed, and free to drain on the surface. In this way, at least, effective drainage is secured, and I can testify that the result may be little short of miraculous.

Using non-fenestrated tubes, I twist them round each day, but do not withdraw them for at least five or six days. By this time a well-defined track is established. I believe heartily in prolonged drainage of all brain abscesses, shortening the tube very slowly and, as it were, reluctantly. As regards the material of drainage-tubes, I should be glad to know whether anyone has experience of the use of decalcified chicken's femora, and of the method of leaving the tube in situ to be absorbed, which Sir William Macewen used to employ. I am inclined to think that the movement and replacement of tubes during the first ten days is responsible for many of the disappointments in cases which appear to be doing well.

In conclusion, I must apologize for the somewhat dogmatic tone of the latter part of the paper. I assure the meeting that it arises from a desire to provoke discussion, and is far from denoting any excess of satisfaction with my own procedure or results.

DISCUSSION (WITH EXHIBITION OF CASES).

The PRESIDENT (Dr. W. Milligan) said the Section was to be heartily congratulated upon having had two such able openers of the discussion as Sir Victor Horsley and Mr. West. Both had put forward points which could not fail to provoke a most useful discussion. Sir Victor's address was pregnant with thought and sound judgment, and it had been a great pleasure to him to listen to it and follow his line of argument, namely, the need for an accurate appreciation of the symptoms presented by the patient, more especially the early examination of the abdominal reflexes, and the question of ocular changes. He had the good fortune to hear Sir Victor Horsley read a paper some time ago before the Pathological Society of Manchester, in which the question of the ipso-laterality of optic neuritis in brain abscess was thrashed out, and since that date the knowledge acquired had been of enormous advantage to him in cases of double otitis media in deciding upon which side an abscess was present, and when to interfere. The initial changes were first noticed on the nasal side of the disk. He regretted that the time at Sir Victor Horsley's disposal did not permit him to enter more fully into technique, as he was so well known as a master of technique. Mr. West's paper, as one would expect, teemed with information of a pathological nature, and in the discussion he asked speakers to pay particular attention to the question of drainage. This was a matter upon which it was desirable to have a consensus of opinion. Besides the question of counter-drainage, which Mr. West had condemned, there was that of drainage of abscess in its acute phase, and the method of drainage in chronic abscess; also whether it was advisable, prior to operation, to undertake lumbar puncture so as to reduce intracranial tension. These points would appeal to members, and he hoped that all present who had anything to contribute to the discussion would do so without hesitation.

Dr. URBAN PRITCHARD showed a case of double cerebral abscess of otogenic origin. The patient was one of the early cases of recovery from brain abscess.

The man was now aged 49, and in September, 1889, was admitted into King's College Hospital under the care of Sir Watson Cheyne and Dr. Pritchard.¹

¹ See *Trans. Med. Soc. Lond.*, 1890, xiii, p. 154.

There was a history of old-standing middle-ear suppuration, with recent severe pain in the left temporal region. On coming into the hospital his symptoms disappeared. There was a polypus in the ear, which Dr. Pritchard removed, and the man seemed to do well. But a few days later there were marked cerebral symptoms, and it was decided to operate. In those days the idea was to go straight for the abscess, and Sir Watson Cheyne removed, by means of the trephine, a large, circular piece of bone behind and above the auricle. Immediately after cutting through the dura mater he came upon an abscess in the temporo-sphenoidal lobe. After this the patient remained in a semi-conscious condition, and about three weeks later he was again operated upon, but no second abscess was found. The practice at that date was to put in a hollow needle and search for another abscess; this was now very properly condemned. A day or two afterwards Sir Watson Cheyne put in a pair of sinus forceps, which, on being opened, entered into the second abscess, which was fairly deep; a drainage-tube was introduced fully 2 in. long, and immediately afterwards the patient began to recover. A few months afterwards a Schwartze operation was done, but this would not be the practice now. For some years following the patient was subject to occasional epileptic fits, an aura in the shape of aphasia warning him of the approach of a fit. He had not now had a fit for five years, and the last was only a slight one on rising in the morning. Practically he had been perfectly well. At times there was a little discharge from the ear, but after syringing out with boracic acid it healed up again.

Dr. DUNDAS GRANT showed two cases: (1) A Case of Temporo-sphenoidal Abscess¹:—

The abscess (1901) was near the surface and readily reached through the squamous bone. There was no definite capsule, so that it was probably of comparatively recent formation. Fætid pus to the amount of about $\frac{1}{2}$ oz. escaped, and the finger introduced into the abscess cavity found the walls to be of soft consistency, collapsing completely upon the exploring finger. A thick india-rubber drainage-tube was introduced into the cavity and very gentle irrigation with boracic lotion was practised by means of a fine-pointed syringe, the tip of which was introduced for a very short distance into the drainage-tube. The pus swarmed with bacilli which gave the staining characteristic of tubercle, but in spite of this very rapid closure took place, and the patient, though still subject to desquamation in the deeper part of the mastoid cavity, is free from all signs of recurrence of her cerebral abscess.

The favourable factor in this case was probably the short duration of the abscess and the absence of anything in the way of a rigid capsule to interfere with the obliteration.

¹ Shown at the Otological Society, February 3, 1902. *Trans. Otol. Soc., U. K.*, 1902, iii, p. 32.

(2) A Case of Cerebellar Abscess secondary to Thrombo-phlebitis of the Bulb of the Jugular Vein. Ligature of Vein and Evacuation of Sinus and Bulb¹:—

In this case exploration of the cerebellum (1905) from the outer surface was in the first instance negative, but a spontaneous evacuation took place through the anterior surface. This, however, was insufficient and the discharge only began to decrease after a large counter-opening was made on the external surface, through which the finger was able to penetrate a well-marked abscess cavity. A drainage-tube was inserted through the outer opening and the discharge speedily subsided. This case, so far as the cerebellar abscess was concerned, seemed to illustrate the advantage of a counter-opening.

Mr. PHILIP TURNER showed the following case:—

A. J., aged 10, was admitted to Guy's Hospital on March 21, 1910, with the following history: For three weeks he had suffered from headache, which was occasionally so severe that he cried out with the pain. During this time he had occasional attacks of vomiting and troublesome constipation. For a few days before admission he had been very drowsy. There had been a purulent discharge from the right ear for some time, but the cause and duration of this were unknown. On admission the boy, though very drowsy, could be roused and then complained of severe pain in the head. The pulse-rate was 52 and the temperature subnormal. The right pupil was dilated and fixed; there was ptosis of the right eyelid and some paresis of the left arm and leg. There was also double optic neuritis. An examination of the right ear showed pus in the meatus, and granulations in the position of the membrane. There was no swelling or tenderness over the mastoid.

At the operation the mastoid cells were found to contain pus and granulation tissue and there was pus in the antrum. A radical mastoid operation was quickly done and it was then found that the tegmen tympani was carious and perforated. The middle fossa was then exposed by removing bone in an upward direction. The dura mater was tense, not pulsating, and its outer surface covered by granulations. Pus in the temporo-sphenoidal lobe was at once found by means of a large needle and exploring syringe. The dura mater and brain were then incised and a large quantity of foul-smelling pus escaped. A drainage-tube was then fixed in position and the lower part of the wound also drained.

A bacteriological examination of the pus showed the presence of *Bacillus coli communis* and a diplococcus, the exact nature of which could not be determined.

On the following day the boy was free from pain and the pressure symptoms had entirely disappeared. In the course of a few days he developed a hernia

¹ Shown at the Otolological Society, February 5, 1906.

cerebri, of considerable size. The superficial part of this eventually sloughed away and the hernia then receded, while the wound granulated and healed, the boy being discharged on May 10.

He attended the out-patient department for some time, feeling well but having a slight purulent discharge from the external auditory meatus. He was lost sight of for some months but was again seen in September, 1911. There was then a large polypus projecting from the external auditory meatus for which he was readmitted. This was apparently attached to the posterior aspect of the meatus but its removal by means of a snare was followed by a gush of cerebrospinal fluid. This continued to escape; the discharge at first was profuse but subsequently diminished and ceased at the end of three weeks.

The boy now appears to be quite well. There is no discharge, and the interior of the meatus shows no granulations.

One remarkable fact is that he hears very well with the right ear. Before the first operation his mother stated that he was deaf, but when first seen it was not possible to ascertain the extent of his deficiency of hearing.

MR. ARTHUR CHEATLE showed seven specimens of chronic middle-ear suppuration which caused, in five instances, temporo-sphenoidal abscess, and in two cerebellar abscess.

In four specimens the mastoid cells were absent, the process being dense in one and diploëtic in three. In all the outer antral wall was dense. In three specimens the type could not be determined owing to operative interference. The specimens demonstrated that the types in which the mastoid cells were absent and the outer antral wall was dense were conducive not only to chronic middle-ear suppuration, but to intracranial complications—a fact which was also borne out by clinical experience.

MR. WAGGETT brought forward, in association with Mr. E. D. Davis, a case of right temporo-sphenoidal abscess, which was operated upon and recovered:—

Female, aged 22, admitted for "headache and drowsiness." Two weeks before admission the patient was suddenly taken ill, with headache and vomiting. She was sent to a convalescent home. The vomiting ceased after the first day, but the headache became more severe. She had a discharge from the right ear, which had continued since an attack of scarlet fever at the age of 5. She states that the discharge diminished about the time she was taken ill. While at the convalescent home she had what she described as a boil in the right ear, which burst. At the end of the fortnight she returned to work, and on the morning of her return and of admission to hospital she is stated to have fallen, and has been drowsy and more or less unconscious ever since.

October 6, 1911: On admission patient is restless, moans, complains of pain in her head: she answers questions intelligently, but it is often necessary

to repeat questions three or four times before receiving an answer. Respiration 24, irregular, and occasionally simulates Cheyne-Stokes breathing; pulse 64, and irregular; temperature 98° 8' F. Pupils: Unequal, right larger than left, react to light, photophobia. Nystagmus on looking to either side. Well-marked optic neuritis; examination by Mr. Treacher Collins. Swelling: Right optic disk, 5D; left optic disk, 4D. Slight rigidity of neck. Paresis of the left side of the lower face, left arm and left leg. Onset of order of paresis not known, it is presumed the face was affected first. Tongue does not deviate; soft palate normal. Knee-jerks increased; ankle-clonus both sides; no Babinski's sign. No superficial epigastric reflex on left. No tenderness of skull on percussion or palpation. Lumbar puncture: Fluid under pressure and contains a few lymphocytes.

October 7: Patient's condition much improved.

October 8: In the afternoon patient gave a sudden cry; relapsed to a similar condition to that on admission.

October 10, 1 p.m.: Patient seen by Mr. Waggett for the first time. Patient *in statu quo*. Right pupil dilated. Weakness of left side of face. Left arm and leg normal. Right ear: Right middle-ear suppuration: granulation, inner wall of tympanum; dropping of posterior superior wall of tympanum; no local tenderness. Operation by Mr. Waggett at 5 p.m.: Right radical mastoid operation. Cholesteatomatous material, and pus in antrum. Tegmen removed; the dura was tense, but pulsation was present. After incision of the dura, sinus forceps was introduced into the brain upwards, inwards and slightly forwards towards the bregma, and at a depth of 2 in. 2 oz. of foul-smelling pus escaped. A rubber drainage-tube was stitched in and left in position for *five days*, not three days as erroneously stated at last meeting, a probe being passed along the tube every day. The length of the tube was 3 in. The tube was cut off flush with the edge of the wound.

Bacteriology of pus: Staphylococci, streptococci and bacilli.

Uninterrupted and rapid recovery. Got up on October 31; left the hospital for convalescent home, November 2.

October 30: Optic neuritis—right optic disk, 1D; left optic disk, 3D. No paresis. Nystagmus still present, but not marked.

December: Patient in good health.

Mr. Waggett said it had been his practice to seek for pus with the median rhinoscopy speculum of Killian, but probably he had missed a certain number of abscesses. On a few occasions he had discovered abscess with his finger when he had failed with an instrument. In an experience of four cases he had never found any deleterious effect from passing his finger into the brain. In one case, that of a woman, the patient was practically dead on the operating table, in the hands of another surgeon, who told him (the speaker) that he could do what he wished. About half her skull was necrosed—a much neglected case

which had been sent in to hospital in a comatose condition. He passed his finger into her brain quite twenty times, and on the following morning she said she had not felt so well for months, and eventually she went out perfectly well. She had no abscess which he could find. He believed the case was reported by Mr. Peyton Beale. In one case with symptoms of cerebellar abscess, he failed to find the abscess on two occasions. On the nineteenth day of the illness the patient became comatose, and he (Mr. Waggett), becoming desperate, passed his finger in and all over one lobe of the cerebellum. He found an abscess the size of half a walnut near the internal auditory meatus. The patient lived for eleven years, and became an inventor.

Dr. A. LOGAN TURNER said that having been conscious of failure in the treatment of many cases of brain abscess, he was anxious to take part in the discussion. He exhibited a table of sixty-eight cases which had been observed in the Ear and Throat Department of the Edinburgh Royal Infirmary during the past six years. His difficulties had consisted first in failure to appreciate properly symptoms and signs which should have led him to operate earlier; and secondly, he had operated upon cases in which there were signs which suggested the presence of a condition which was not actually found. There were one or two diagnostic points which he had tried to work out in an analysis of these cases. He was sorry that the ophthalmoscopic appearances had not been worked out in detail, especially after what Sir Victor Horsley had said; but he had very fair notes on that head, and would look into the matter again. The table of incidence was interesting from the point of view that localized brain abscess evidently occurred much less frequently than did sinus thrombosis and meningitis. There were twenty-two cases of localized brain abscess, whereas sinus thrombosis and meningitis occurred fifty-eight times. There was also a greater frequency of uncomplicated localized brain abscess, while sinus thrombosis and meningitis occurred relatively more frequently along with some other complication. This was in favour of more successful treatment in localized brain abscess. There were eleven cerebellar as opposed to eight temporo-sphenoidal abscesses. With regard to headache as a localizing symptom, in eight cases of temporo-sphenoidal abscess, and in two cases in which a large extradural abscess was in the middle fossa, there was temporal headache in seven, frontal headache in two, and in one the situation was not stated; whereas in eleven cerebellar abscesses the headache was frontal in seven, vertical in one, occipital in one, and

in one it was absent. In one the position was not stated. Of five cases of abscess in the left temporo-sphenoidal region, in four there was visual aphasia, inability of the patient to name objects, which was a useful sign in diagnosis. In eight cases of left cerebellar abscess that sign was not present. The other points investigated were vertigo and nystagmus. In the temporo-sphenoidal cases there was vertigo in one; no vertigo in eight. There were seven with no nystagmus, two with nystagmus, and in one no notes had been made. Of the two with nystagmus, however, there was inner ear disease in one, and in the other an extradural abscess was also present in the cerebellar fossa. The opposite was the case in cerebellar conditions, for of the eleven cerebellar cases there was vertigo in seven. Two patients were too ill for this to be ascertained, in one it was absent, and in one there was no note. Spontaneous nystagmus was observed in eight. With regard to the direction of the nystagmus, it was in both directions in five of the cases, with a tendency for greater intensity towards the affected side. In two it was to the affected side only, and in one to the normal side. The incidence of the nystagmus varied in the cerebellar cases; sometimes on examination one found no nystagmus, at other times it was present. With regard to the class of case in which there were signs and symptoms suggesting a certain complication but in which another condition was found, he wished to refer to one case which suggested meningitis in the posterior fossa, but in which a cerebellar abscess really was present. There was excessive turbid cerebrospinal fluid, an increase of albumin in the fluid, no reduction with Fehling's solution, and a large excess of polymorphonuclear cells. The temperature was high, the pulse-rate rapid, there was rigidity of the neck, double Kernig's sign, leucocytosis 22,000, a history of vertigo, and nystagmus in both directions. The case was treated for meningitis—i.e., a radical mastoid operation was done and a series of lumbar punctures carried out. Four days after admission the patient died suddenly. On post-mortem a large cerebellar abscess was found lying close to the surface of the lobe and leaking into the meningeal spaces through a small aperture. No meningitis could be detected macroscopically. With regard to lumbar punctures, he was in the habit of performing that as an aid to diagnosis. In the case recorded it had proved rather a disadvantage than an aid to diagnosis; the knowledge gained by the procedure might not always be helpful. He regarded accurate diagnosis as a most important factor in the successful treatment of intracranial complications.

Mr. HERBERT TILLEY said he would like to hear from Sir Victor Horsley what was the relative frequency of post-operative Jacksonian epilepsy. He had met with it in one case of cerebral abscess, which Sir Victor Horsley would remember. That patient developed epilepsy after evacuation of a temporo-sphenoidal abscess, and his aura was a sensation of a foul smell. Any suggestion from Sir Victor as to how such irritative lesion was probably produced would be gladly welcomed. With regard to drainage, he had always used a tube. He could not conceive any one using a gauze drain for any wound, especially a cerebral one: an open pipe was required, not a wet plug. Anyone who considered the manner in which the wound exudation quickly soaked the gauze drain would appreciate this view. He of course meant that the tube should have a definite calibre equal to that of an ordinary lead pencil.

Mr. HUGH JONES (Liverpool) said he did not know whether Sir Victor Horsley wished the Section to understand that never was there a rise of temperature from the beginning in cerebral abscess. He had had two or three acute cases in which there was a definite initial rise of temperature. Was that due to the concomitant condition, or to the lesion of the brain? Many years ago he appealed unsuccessfully to several authorities to tell him what were the symptoms of latent brain abscess, as one often felt instinctively that abscess was present and there should be something to indicate it; there were clinical signs present, but we could not see them. Sir Victor Horsley had now brought forward a number of those fine delicate symptoms in the difficult latent stage, to which attention had not previously been paid, especially in regard to loss of sensation or difficulties in discriminating between points of contact, and the changes in the reflexes. Did Sir Victor Horsley wish all mastoid cases to be investigated in the same way? With regard to optic neuritis; the first case of brain abscess he had operated on (nineteen years ago) was a distinct case of the kind referred to (latent abscess). There was optic neuritis of the left eye, and the diagnosis was to some extent based upon the fact of ipso-laterality of the optic neuritis, though it was helped by the fact that the patient also had some aphasia. The patient had left temporo-sphenoidal abscess, which did very well. Drainage and searching for the abscess had been his greatest difficulty. At the Edinburgh meeting Mr. Ballance insisted on the use of the knife as a searcher, saying that one might feel round with a blunt instrument and yet miss an abscess, whereas a sharp knife would not only do less

harm but would be more certain to find the abscess and penetrate its wall. He (Mr. Jones) had found that the less one interfered with the abscess after it was drained the better. Drainage he found best carried out by putting in a double tube and keeping it there. But sometimes he found it difficult to know whether to shorten it or not. Two or three months ago he operated upon a patient who was apparently doing very well, but one night, in the temporary absence of the night nurse, she got out of bed and fell, and though put back to bed apparently without harm, was found dead in bed next morning. He could not obtain a post-mortem examination, but he assumed that the abscess had burst into the lateral ventricle. It was possible that the fall, by pushing the tube too far in, had caused the mischief. He, with Mr. West, had always favoured the natural route in acute cases and where a distinct track existed, but several speakers at Edinburgh said that that was unsurgical, especially where there was any doubt about the diagnosis; they said it should be a clean opening in an absolutely fresh surface, so as to avoid the possibility of infecting any other part of the brain. In cerebellar abscess he favoured the anterior route (internal to sigmoid sinus), with a secondary counter-opening.

Mr. HUNTER TOD said he was much interested in what Sir Victor Horsley had said about optic neuritis, because recently two such cases had been under his care at the London Hospital, and the question was raised whether operation should be performed on account of a suppurative intracranial lesion, or whether the patient was recovering from meningitis, or internal-ear inflammation. In one of the cases, there had been acute middle-ear suppuration, and the patient had been sent to the hospital under the belief that there might be a brain abscess. Before admittance there had been pyrexia, vomiting, and head retraction, but the ear was now seen to be almost dry. Mr. Lister found, on examination, early optic neuritis, with marked œdema of the optic disk, amounting to +5D on the same side, and very slight optic neuritis on the other side. As there were no localizing symptoms, and as the middle-ear suppuration had ceased, it was decided not to operate. In spite of the patient's general condition remaining normal, optic atrophy began to be manifest on the affected side. In the other case, one of chronic middle-ear suppuration, there was very marked œdema of the optic disk, followed rapidly by optic atrophy on the same side, so that within six weeks it seemed that the eyesight might eventually be lost; on the other side a similar condition, to a much lesser extent, was taking

place. The mother of the patient refused to permit operation, but the child, however, is now perfectly well with the exception of the eye changes. These cases raised the question as to whether one should operate, and to what extent, in middle-ear suppuration with optic neuritis, even although there was complete absence of all the intracranial symptoms. These cases also supported Sir Victor Horsley's view that the presence of marked œdema of the optic disk on the same side as the aural affection favoured the diagnosis of meningitis rather than an intracranial abscess.

Mr. Tod said he remembered a case in which neglect to operate, owing to expectant treatment being carried out as there were no localizing symptoms, resulted in the sudden death of the patient from the bursting of a cerebellar abscess. In Mr. Tod's view the question of when to operate in these cases, and to what extent, seemed a most difficult problem.

With regard to technique, he considered that the complete mastoid operation should first be performed, and then that only as much bone should be removed from the tegmen tympani and lowest portion of the temporal bone above, or from the mastoid behind, so as to expose the brain sufficiently to insert a large drainage-tube. The cases in which he had been successful were those in which all the classical symptoms were present. In cerebellar abscess his results had been bad, as out of ten cases there were only two recoveries. In no case had recovery taken place in which drainage was attempted by the anterior route.

He wanted to call attention to a condition, probably encephalitis, the symptoms of which closely simulated intracranial abscess. In this type of case all the symptoms of intracranial pressure occurred, usually very rapidly, and were accompanied by an irregular and slight pyrexia. Pyrexia was a bad sign, whether abscess was found or not. On incising the dura mater the brain substance projected from the wound, being usually very congested and friable. If the patients died, they did so within a few days from coma or from meningitis. With the above symptoms, if no abscess were found on exploring the brain, Mr. Tod urged that more bone should be removed and the brain substance incised in several directions. In some cases, as in Mr. Waggett's case, the results were most satisfactory, and complete recovery took place.

In one case, which had all the signs of intracranial pressure together with visual amnesia, a temporo-sphenoidal abscess on the left side was diagnosed. No abscess was found, but definite encephalitis. Much

bone was removed, with a resulting large hernia. Recovery took place slowly, with loss of visual amnesia. Three weeks after the operation all the symptoms returned. A fine pair of sinus forceps were then pushed into the brain, and an abscess found. Whether the abscess was the result of exploration or encephalitis is a matter of conjecture. The patient eventually recovered completely, and is now at work again. If it were known why patients died two or three weeks, or even later, after an apparently successful operation, the methods of treatment might be improved from that point of view. He found meningitis was most common in cerebellar abscess. In other cases there were shock and coma, which he attributed to oedema of the brain.

Mr. Tod also asked Sir Victor Horsley what should be done for epilepsy developing after an operation. He had one such case, upon which he had operated six years ago. He had removed a large area of bone, and at the first dressing the patient had an attack of typical Jacksonian epilepsy. This man had done very well, but he had recurrent attacks of Jacksonian epilepsy at long intervals.

Dr. A. BRONNER asked how one was to know what vaccine to use when the organisms were so varied; also what pus-searcher Sir Victor used. He now used the one recommended by Mr. West, but with a small abscess having a thick wall one was not so likely to open it up with that as with Macewen's. He asked Mr. West what became of the capsule—was it absorbed? If there were many pneumococci present the capsule was generally thick, whereas if there were few it was thin. With regard to the eye symptoms, most members would have read Sir Victor Horsley's researches on this matter. Eyes varied very much physiologically; one eye would often show more venous congestion than the other. In many cases of hypermetropia, &c., the disks were congested and there was also intense headache. The use of glasses relieved the symptoms at once. He always opened up as suggested by Mr. West, and asked what method Sir Victor adopted. He believed that usually not enough bone was removed. One should remove a large piece of bone outwards, so as to get drainage downwards and outwards.

Mr. SYDNEY SCOTT said that the topic was a fascinating one. Every case of brain abscess was a subject for careful study in itself. In considering the factors conducing to successful treatment he thought it was

important to realize what the mortality of brain abscess was. Some years ago he collected from the post-mortem records at St. Bartholomew's Hospital all the fatal cases of ear disease during a period of ten years, beginning with his first connexion with the Hospital and including cases which he had not himself seen. Not finding time to work at this material in a way he wished, he induced his late assistant, Dr. Tyler, to investigate the subject afresh. Dr. Tyler collected the post-mortem records of all the fatal cases of intracranial infection in St. Bartholomew's Hospital during a period of sixteen years (October, 1895, to October, 1909).¹ He (Dr. Tyler) found that during this time there were six hundred and forty-four cases of intracranial infection: of these two hundred and sixty-seven were directly traceable to the ear (after excluding such cases as tuberculous meningitis, in which there also happened to be otitis media, and other cases in which ear disease could not be regarded as a causal agent). Of the two hundred and sixty-seven cases of otogenous intracranial infections in one hundred there was leptomeningitis; in fifty-five lateral sinus thrombosis; in forty-two brain abscess; in thirty-four extradural abscess, and the rest presented miscellaneous conditions. Taking the forty-two cases of brain abscess, thirty were temporo-sphenoidal and twelve cerebellar. Dr. Tyler's figures are of post-mortems only; they do not include patients who recovered after operation, or cases of supposed brain abscess in which no post-mortem examination was made.

Mr. Scott had looked up the cases of brain abscess admitted during the fourteen years previous to 1911. Fifty-two patients were admitted, and he could only find that some ten cases were treated successfully. Dividing this time into two periods, during the first seven years, twenty-six cases were admitted and twenty-four died, mortality, say, 95 per cent. One case of recovery was that of a cerebellar abscess which was irrigated. Another case of temporo-sphenoidal abscess, which recovered and lived (for two or three years, ultimately dying of a relapse, therefore included among the fatal cases), was tube-drained for sixty-two days. During the second period of seven years, again of twenty-six cases admitted, eighteen died, mortality, say, 75 per cent. In the last three or four years there had been a further slight diminution in the mortality.

Of factors which conduce to success, he believed it would be generally admitted that specialization was an important one. Secondly, by careful

¹ "The Paths of Encephalic Infection in Otitis." Thesis for Cambridge M.D. by Christopher Tyler.

attention to the neurological survey, for which they owed so much to Sir Victor Horsley, he believed that exploratory puncture of the brain for purely diagnostic purposes was less frequently called for. Thirdly, in puncturing the brain, special care should be taken thoroughly to disinfect the area exposed. Fourthly, he believed a free incision should be made in the dura mater, and that the puncture should be made for preference with a narrow straight knife, inserted at right angles to the dura mater. Lastly, with respect to drainage, when an abscess was found, he was beginning to think that a free incision into the abscess should generally suffice, for from a consideration of cases which had recovered, he felt sure they recovered in several cases in spite of drainage-tubes and in spite of gauze or other mechanical devices; in fact the brain (except, in the case of a deep-seated or encapsuled abscess), after having been well incised, drained itself. But even with every attention and care, he submitted that brain abscess would always claim a high mortality on account of anatomical conditions, and the most practical way to lower that mortality was to diminish the incidence of the disease. This he believed was being done by the increasing numbers of mastoid operations, and more efficient treatment of ear suppuration; so that a time might probably come when abscess of the brain due to disease of the ear would be more and more rarely met with.

The PRESIDENT said the factors which conduced to success might be divided into two main classes: First, an accurate appreciation of the clinical signs and symptoms as detailed by Sir Victor Horsley; secondly, an accurate interpretation of those pathological facts which Mr. West had dilated upon. On thinking over what had been said at the meeting, it would be found that much had been learned from the discussion, though, perhaps, it might have been more concentrated on the factors conducing to success. He had often had great difficulty in diagnosing and treating intracranial abscess, especially from the point of view of maintaining successful drainage. While again thanking Sir Victor Horsley and Mr. West for their contributions to the subject, he would like to include in that expression appreciation of Dr. Logan Turner's remarks, which would be of great service in connexion with the papers read, and would serve as material for reference in the future.

Sir VICTOR HORSLEY, in reply on the debate, said that the route to be followed depended on the case. He agreed with Mr. West that if there was destruction of the tegmen one should enlarge that opening.

On the other hand, if there was not he was emphatically of the opposite opinion. He thought one should explore the parts which were being investigated as aseptically as possible, and therefore he used the trephine freely. With regard to pus-searching, he had himself invented a pus-searcher twenty years ago, and he still used his own instrument. Killian's consisted of much the same thing, namely, two directors. The moment pus came out one slipped in the tube. With regard to drainage, he sympathized with his colleague, Mr. Tilley, and if he (Sir Victor) expressed himself in equally strong language about gauze he hoped he would not be misunderstood. He did not believe in draining the brain with gauze, nor did he believe in leaving the brain to drain itself. He used a concentric tube. He took a tube of $1\frac{1}{2}$ cm. in diameter, split it down, and then pushed down it another tube 1 cm. in diameter. He sewed the split tube into the cavity by stitching it into the dura, and it was not moved for a long time. He agreed that drainage ought to be kept up. With regard to the question whether one was justified in doing this in the case of an acute abscess, or whether one should leave an acute abscess alone, he had never had sufficient courage to leave one alone after emptying it; possibly it might be due to a lack of enterprise. Obviously some could be left alone. He had always washed them out. Most infections had been mixed. With regard to infections, the two cases he showed that afternoon were very easy cases to deal with from the vaccine point of view, because in the case of the little girl the infection was a pure streptococcus culture; and in the man's case it was an infection by three organisms, but among them one easily found and isolated—the *Staphylococcus aureus*. The first influenzal cerebral otogenic abscess he had to deal with contained five organisms, and nothing was isolated which he could prove, by inoculation into animals; to be the cause of the disease. He agreed with Dr. Davis that hernia cerebri would get well. But this being associated with the infection of tissues with organisms, in his experience it got well more quickly if one painted it with pure carbolic acid. With regard to eye symptoms, he disagreed with the practice of leaving meningitis cases untreated. If a child came with optic neuritis, and went out of the hospital practically blind, it was a grave reflection upon the medical men concerned. Of course, where operation was refused, the responsibility of the surgeon did not exist. He believed that all cases of otitis media with optic neuritis ought to have a very free operation done on the mastoid, and if the neuritis did not subside in a short time, the subdural space should be opened by a

separate operation above. He had done this with excellent results. The moment the skull was opened the neuritis disappeared, and to allow it to go on to secondary atrophy was a very serious matter. With regard to lumbar puncture, he agreed with what Dr. Logan Turner said—that one could not always interpret what one found by the test, but he did not agree that they were better without the knowledge, as he believed that all knowledge was useful. The President had thrown more light upon lumbar puncture in these conditions than had anyone else, and he regretted that the meeting had not heard Dr. Milligan upon it. In the same breath he both congratulated and condemned his friend Mr. Waggett, because although he had proved to demonstration that digital treatment of the brain was excellent for some people, he (Sir Victor) did not believe it was beneficial on the average. He fully agreed with those who said that although the brain should be exposed widely it should be touched as little as possible, and then only with sterilizable materials, and with as little bruising as possible. He had never seen a pus-searcher fail to strike the pus; he had seen it strike against a thick sac, which sac he had removed *in toto* by pulling it out, not as a *dernier ressort*, but as a deliberate operative procedure.

Mr. WEST, in reply, said the pulse showed a certain particular quality in the majority of cases of brain abscess. It was a large, soft, and delayed pulse; it showed a long heaving wave, which could be compressed so that one could easily obliterate the pulsation, and it impressed one as being really slower than counting showed it to be. When it seemed to be 55 it might really be 65. With regard to temperature, it would be agreed that in otitic brain abscess there were many cases in which the abscess was surrounded by much encephalitis, with raised temperature; but the pulse was slow relatively to the temperature. One might find a child with a temperature of 103° F., and the pulse of about 80. On the other hand, there were patients whose temperature was very low. With regard to cerebellar abscess, there was a character of the knee-jerk which had not been dwelt upon. In one or two cases which he could recollect the patient was comatose, and the knee-jerk was extraordinary; it was really a spasm followed by clonus, the leg being held in the extended posture for some seconds, and was probably due to direct pressure on the pyramidal tract cutting off all control from the upper centres, so that the lumbar centres could do as they liked. Referring to Dr. Logan Turner's case of cerebellar abscess, probably it would be agreed that in many cases of cerebellar

abscess lumbar puncture showed an excess of cerebrospinal fluid which was cloudy and crowded with polymorphonuclear leucocytes, but was sterile. Cerebellar abscess showed retraction of the neck also. He believed Dr. Logan Turner's case did not ooze and so produce the cloudy meningeal fluid, but oozed comparatively late as the result of the repeated withdrawal of the support of the thin outer wall of the cerebellar abscess by lumbar puncture. Years ago he maintained, at the Otological Society, that one might burst an abscess by diminishing the pressure which had been supporting its thin wall. Cases of late death after operation often occurred; in some of them one could not tell the cause of death—some had late infection of the ventricle, and others a spreading infection of the brain. In some cases it was a question of rash and rough manipulation of drainage-tubes, and that was why he raised the question about decalcified bone tubes which could be left in indefinitely without breaking up the surrounding brain. With a thick capsule, such as he showed, the cavity would, he believed, never become obliterated. But the ordinary abscess wall consisted of immature scar tissue, and if the cavity could be obliterated, the whole area would become a mere scar in the brain substance.

Otological Section.

February 16, 1912.

Dr. W. MILLIGAN, President of the Section, in the Chair.

Severe Labyrinthine Vertigo (Ménière's Disease ?) ; Operation ; Recovery.

By W. MILLIGAN, M.D.

PATIENT, male, aged 40. Sudden attack of vertigo, accompanied by sickness, tinnitus, and complete loss of hearing upon the affected (left) side five years previous to admission to hospital. During the past five years attacks of vertigo have been frequent and have increased in severity despite general and local medicinal treatment (Dr. Malim, Rochdale). Admitted to hospital on account of constantly recurring and severe attacks of vertigo, tinnitus, and sickness, preventing the carrying on of his occupation. General health good ; heart and lungs normal ; no arterio-sclerosis. Urine normal.

Left ear : Membrana tympani opaque and slightly retracted. Complete deafness. Tuning forks (high and low tones) not heard upon left side—referred to right ear. Marked Rombergism. Caloric test (cold water, 20° C.) : Nystagmus induced in 70 seconds.

Operation (July 20, 1911) : Complete "bridge operation" performed ; severe prostration for twenty-four hours, then gradual improvement and cessation of sickness.

July 30 : Vertigo entirely relieved ; tinnitus about the same.

January 29, 1912 : Patient expresses himself as feeling perfectly well. No attack of vertigo or sickness since operation, six months previously. Tinnitus still present, but not nearly so loud and distressing. Left ear absolutely deaf. Caloric tests : No reaction upon affected side up to 150 seconds with hot water (42° C.) and cold water (20° C.) ; upon healthy side reaction induced with hot water in 90 seconds, and with cold in 70 seconds.

Suppurative Labyrinthitis, complicated with Suppurative Basal Meningitis; Operation, Translabyrinthine Drainage; Death.

By W. MILLIGAN, M.D.

PATIENT, female, aged 36, deaf mute. Scarlet fever at age of 2½ years. Left ear suppurated since. Admitted to hospital on account of increasing vertigo and facial paralysis of three days' duration.

Left ear: Large perforation; cholesteatoma (?); very foetid discharge. Caloric tests negative; no "fistel" symptom.

Right ear: Membrane opaque and retracted. Caloric tests: Slight reaction (cold water, 20° C.) after 90 seconds. No optic neuritis. Knee-jerks normal; no ankle-clonus. No Babinski's sign; no Kernig's sign. Blood count: Leucocytes, 6,000.

For the first four days after admission patient apparently well; upon fifth day a rise of temperature to 100° F.; discharge from ear profuse and very foul. Temperature next day, 101° F. Following day patient became suddenly unconscious; temperature, 101.4° F.; severe vomiting.

November 27, 1911: Operation decided upon. Preliminary lumbar puncture; fluid turbid and under high tension; no organisms. Complete post-aural operation performed: Cholesteatoma found and removed; facial nerve found exposed; external semicircular canal black, necrotic, and perforated, admitting the point of a Dundas Grant's antrum hook. Removal of internal ear and opening up of internal auditory meatus. Dura mater incised; escape of about one teaspoonful of pus and much cerebrospinal fluid. Operation area disinfected with Lake's strong antiseptic fluid. Translabyrinthine drainage instituted.

November 28: Consciousness returned. Temperature fell to 99.6° F.; pulse 70. Lumbar theca again tapped. Fluid turbid, alkaline, large coagulum, reduced Fehling's solution; albumin increased, no globulin; increase of polymorphonuclears; a few diplococci in films.

November 29: General condition much improved.

December 5: Severe headache complained of. Temperature, 102.8° F. Lumbar puncture again performed. Fluid turbid and under high tension; no organisms. Attack of acute otitis media upon right side.

December 9: Sharp attack of diarrhoea (septic ?); mastoid wound appears healthy.

December 11: Temperature rose suddenly to 103° F.; slight retraction of head.

December 14: Condition generally unsatisfactory; 40 c.c. of cerebrospinal fluid withdrawn; turbid; excess of polymorphonuclears; albumin increased; no globulin. On culture of both fluid and coagulum no organisms found. Opening towards base of brain enlarged; opening in dura also enlarged and double drain inserted.

December 16: Condition improved. Quite conscious; pulse good.

December 17: Rise of temperature to 102.6° F.

December 19: Lumbar puncture again performed. Fluid almost clear; polynuclear leucocytosis; no organisms. Blood count, 7,000 white cells.

December 30: Patient going on very well. Quite conscious, and taking food well.

January 9, 1912: Not so well; pain around vermiform appendix. Temperature normal.

January 10: Temperature, 101.6° F.; patient semiconscious. Lumbar puncture again performed. Fluid almost purulent and full of staphylococci and streptococci; profuse perspiration and flushed face. Sudden maniacal symptoms, followed by coma and death.

Autopsy.—Brain very oedematous; extensive basal meningitis, and, upon left side, a large amount of free turbid fluid. Drainage across the pars petrosa found accurate; brain opposite internal auditory meatus coated with thick purulent exudate.

Opinions invited as to whether in such a case it would be advisable, in addition to translabyrinthine drainage, to perform an extensive decompression operation.

Dr. Milligan also showed a sequestrum showing semicircular canal system from a case of suppurative labyrinthitis in a boy, aged 14.

Three Cases of Operation on the Labyrinth for Vertigo (Non-suppurative).

By HUGH E. JONES.

CASE I.

J. B., AGED 40; out-patient, March 22, 1907.

History: Deaf ten years; last three weeks has not been able to walk without stooping and using a stick on account of giddiness. Had giddiness also nine years ago. Had discharge from left ear for five years, ending nine years ago. Says he has been more or less

light-headed ever since. Was under Mr. R. Williams's care at Myrtle Street Eye and Ear Infirmary.

Condition: Post-nasal catarrh; "deaf voice"; left tympanum disorganized (?); and membrana tympani cicatricial.

Hearing: Watch—right, *nil*; left, *nil*. Tuning fork, B.C.—right, *nil*; left, *nil*; A.C.—right, ?; left, ? Voice—right, very loud close to ear; left, *nil*.

Treatment: Potas. iod., 10 gr. t.d.s.; mustard plasters daily over left mastoid. May 17, 1907: Note, "? destroy labyrinth." June 7: Ung. hydrarg. oleat., 10 per cent. September 13: Mist. K.I. October 25: Note, "Inclines to fall forward and has clockwise (from observer's point of view) rotation of objects; no spontaneous nystagmus. January 3, 1908: Iodipin. March 13: Valyl capsules. None of the treatments applied appeared to afford any relief.

June 10, 1908: Admitted into hospital.

June 20: Complete post-aural operation. Left external semicircular canal opened and curetted up to the ampulla; vestibule not curetted.

July 24: Discharged from hospital.

During the ensuing year the patient (after the first three weeks) was able to walk about without a stick and was evidently very much better, but never admitted that he was wholly free from giddiness.

June 4, 1909: Return of giddiness; granulation growing over the external ampulla.

June 18: Cavity completely healed again. Since the last date there has never been any discharge from the ear.

August 13, the following note was made: Bone conduction, doubtful perception in either ear. Edelman-Galton—right, 5.6 mm.; left, *nil*. Caloric test—hot water, no nystagmus either side; cold water, right, no nystagmus; left, five or six slow movements.

Remarks.—I have not been able to determine the cause of the deafness in this case, but it seems to me to be suspiciously like a syphilitic one. The suppuration in the left ear had not left much evidence of its presence. There was a cicatrix in the membrana tympani, and possibly some adhesions, but no destruction of ossicles or bony walls. The result of operation seemed to be at first a definite improvement. This was not admitted by the patient, but all who saw him walk said that he was much steadier on his feet, and it was noticed that he did not walk with his hand on the wall and that he had given up using a stick. He was suspected after the operation, perhaps unjustly, of malingering, and had for some time been drifting into a condition of neurasthenia.

CASE II.

Mr. W. W., farmer and milk dealer, about 40 to 45 years of age, was sent to exhibitor by Dr. Given, Mossley Hill, on November 30, 1908.

History: Buzzing in left ear for ten or eleven years. Attack of Ménière's symptoms seven or eight years ago. Slight attacks of dizziness at intervals ever since. Intervals shorter lately. Buzzing and hearing are worse for two or three days before an attack. Attack lasts about three hours; everything goes round in a vertical plane. Never falls, but has to lie down. Right ear little if at all affected; slight scaly eczema of meatus. Some nasal catarrh at times. No lobules to auricles (jug-handle ears).

Condition, November 30, 1908: Membrana tympani practically normal; good mobility. Eustachian tubes patent. Slight scaly eczema of right meatus. Hearing: Acoumeter—right, 4 ft.; left, 4 ft. Tuning fork—right, B.C. full?; left, $\frac{3}{4}$. Rinné—right, positive; left, positive. Galton—right, 1 mm.; left, 1.5 mm. Opinion expressed that, as hearing returned after each attack, the attacks might be considered as of "functional" origin. The "jug-handle" shaped pinnæ seemed to support this view.

May 13, 1911: On this date Mr. W. was again sent to me by Dr. Given. During the interval of two and a half years several slight attacks had occurred; Mr. W. had been able to carry on his business, but during the last few weeks the deafness had been increasing, the tinnitus had been constant and annoying, and several minor attacks of the Ménière type had occurred. On May 12 (yesterday) Mr. W.'s troubles culminated in a violent attack while he was lying on a sofa reading. He suddenly felt as if he and the sofa were being rolled over and over to the right side. Mr. W. said that he clung tightly to the sofa, and that the whole affair seemed to him very horrible. The main attack was followed by dizziness and vomiting. Mr. W. said he could not trust himself to drive in his milk float, and that he was prepared to submit to any operation which gave a reasonable chance of relief. He was quite ready to sacrifice the hearing of the left ear, but hoped to be rid of the tinnitus at the same time. Nothing new was noted about the appearance of the ears. Hearing: Acoumeter—right, 10 ft.; left, 3 ft. Tuning fork—Weber, equal. B.C., right, -5 seconds; left, -15 seconds. Rinné—right, positive; left, positive. Galton—right, 0.2 mm.; left, 1.4 mm. Ten seconds

difference between the two sides tested against one another. More details of tuning fork reactions appended.

AIR CONDUCTION (HARTMANN'S SMALL SET OF FORKS).

Forks	Heard by observer, H. E. J.		Patient's right ear		Left ear	
C
C 124	...	70 seconds	...	50 seconds 5/7	...	35 seconds 1/2
C ¹	...	65 "	...	50 " 5/6.5	...	40 " 4.6.5
C ²	...	60 "	...	50 " 5.6	...	20 " 1.3
C ³	...	40 "	...	30 " 3/4	...	20 " 1/2
C ⁴	...	12 "	...	12 " 1/1	...	7 " 7/12

As a consultation could not be arranged, and no friend was present, I refrained from applying turning and caloric tests.

May 26, 1911: Operation—Inner wall of antrum exposed without removing "bridge" or touching the tympanum; external semicircular canal opened and posterior limb followed, posterior and superior canals burred away, vestibule not entered. Thin gauze drain. Tympanum and vestibule were not interfered with because hearing was relatively good.

After-history: No reaction or shock, no vomiting or spontaneous nystagmus. Dizziness on sitting up or moving head suddenly. Stitches and drain removed fourth day. Tinnitus unaltered. Recovery was uneventful.

February 6, 1912: After the first dressing I did not see Mr. W. again for several weeks. Caloric reaction was then negative on operated side, positive on the other. Turning reaction: No satisfactory record, both weak (only one trial made). Hearing and tinnitus unaltered. Dr. Given reported on this date (February 6) that the patient has been quite well since convalescence was completed in July last.

Dr. Given has promised full notes of the case, but they are not yet to hand.

CASE III.

E. L., married woman, aged 32. Admitted as an out-patient on December 13, 1911. Left ear deaf six months; buzzing tinnitus one month; giddy attacks twice a day, lasting about three-quarters of an hour. Does not fall, but has to sit or lie down and hold on to things; during attack things whirl round. Vomiting.

December 13, 1911: Watch—right, 18 in.; left, *nil*. Tuning fork—right, B.C., full; left, B.C., *nil*; A.C., $\frac{1}{4}$. Caloric reaction—left

(cold) induction, 50 seconds; duration, 90 seconds; right (cold) induction, 70 seconds.

January 10, 1912: Superior vestibulotomy, after opening and following the anterior limb of the external semicircular canal. Tympanum not touched, and "bridge" not removed. After-history: Vomiting and dizziness on movement for three days. Tinnitus disappeared from first day. Wound healed by first intention, except for thin gauze drain, which was removed with the stitches on the fourth day. Highest temperature, 99.2° F.; pulse, 64 to 80. Patient was able to walk across the ward about the tenth day. Discharged January 27.

January 24: Tuning fork, *nil*. No tinnitus since the operation. Caloric reaction (cold)—right, induction 60 seconds to 70 seconds; left, negative. Turning—left, no reaction.

January 31: Walks unsteadily, with tendency to fall to the left; cannot stand for more than three or four seconds on either foot singly.¹

REMARKS.

The notes are unfortunately far from complete, especially as regards vestibular reactions.

In the first case (J. B.) the external semicircular canal was the only part of the labyrinth destroyed. Relief incomplete; tinnitus continued; hearing not restored, giddiness said to have returned (this is doubtful). ? other ear.

In the second case (W. W.) three semicircular canals destroyed, vestibule and tympanum not touched. Relief from vertigo complete, tinnitus remained; hearing neither better nor worse.

In the third case (E. L.) external semicircular canal and contents of vestibule destroyed. Tinnitus stopped, hearing worse, some titubation remains.

In no case was there any rise of temperature, and, except in the last case (a woman), no shock to speak of.

¹ February 21: Tinnitus has returned; some titubation remains, but no attacks of vertigo have occurred. March 6: Much improved as to gait and tinnitus; no further vertigo and no spontaneous nystagmus.

**Labyrinthine Vertigo (Mènière's Symptoms—Non-infective)
treated by Operation.**

By G. J. JENKINS, F.R.C.S.

THE patient, a woman, aged 24, had previously been shown at a meeting of the Section held in May, 1911, and a report of the case was published in the *Proceedings*.¹

DISCUSSION.

Mr. G. J. JENKINS, referring to his own case, said that before the operation the patient complained of Mènière's symptoms—severe attacks of vertigo with nausea and vomiting, impairment of hearing (C.V. at 3 ft.) and severe tinnitus. The operation done was the draining off of the perilymph by opening the external semicircular canal without injury of the membranous canal. The patient was very collapsed for a few days after the operation, but gradually recovered, so that in three weeks there was no vertigo, conversational voice could be heard at 15 ft. and the tinnitus was very slight. This improvement has been maintained. There have been no attacks of vertigo, conversational voice can be heard at 15 ft. to-day, and the slight tinnitus does not annoy the patient. Rotation tests applied to-day show diminished reaction to clockwise movement, but also slight for contra-clockwise rotation. Caloric test—cold water—gives very fine horizontal and rotatory nystagmus in both ears, but slightly less marked in left ear. She can now do her ordinary work as a cutter in a workshop. Mr. Jenkins referred to the somewhat analogous condition of glaucoma. In glaucoma there are flashes of light, &c., and in a case of Mènière's symptoms there is a similar aberration of the functions of the ear in the tinnitus and vertigo; in glaucoma there is defective vision, and in Mènière's cases there is defective hearing and also defective vestibular sensibility; in glaucoma there is often nausea and headache and also similarly in cases with other Mènière's symptoms.

Mr. RICHARD LAKE said, however hard one tried it was very difficult to lay down principles on which to operate. His first case was that in which most hearing was preserved, and in that he did not destroy the vestibule. He did not understand how Mr. Jenkins could expect an increase of fluid in a bony compartment. In the cases he had seen there was no appreciable increase of fluid; yet in view of the relatively short duration of Mr. Jenkins's case it was possible that there was a hyper-exudation of fluid. The operation more applicable for such cases would be Neumann's—i.e., to open the posterior canal instead of the external.

¹ See *Proceedings*, 1911, iv, p. 116.

Mr. C. E. WEST desired to congratulate all concerned in these cases on the fact that the patients had survived the operation, and with such a satisfactory result. But he would like to caution his hearers against regularly operating for non-suppurative labyrinthine vertigo; for a large majority of those cases under dieting and medical treatment would get well without operation. Years ago he thought that if one waited one would be obliged in the long run to operate on many of these cases; but he had not yet met one case in which he had been forced to do so. He admitted, however, that in such skilful hands as those of Mr. Jenkins, the President and Mr. Hugh Jones, the results were satisfactory. A few days previously he heard of a case in a gentleman, aged 50, whom he saw last May, and who was incapacitated at that time by violent recurrent vertigo. He did not press operation upon him, but placed it before him as a last resort if he did not get better. That day he heard that the patient had not had an attack since last July. Had he been operated upon in May his position would not now have been better than it was to-day. Judging by cases in which the labyrinth was suddenly broken up, by disease or by operation, he would have had a long period of inco-ordination and helplessness and would have lost hearing in that ear, whereas now he had very useful hearing. He believed the wise attitude was that of a reluctance to operate.

Mr. WESTMACOTT said it would be interesting to know when the operation should be done and when it should not. Some of the cases were very severe, and, especially in brain workers, prevented the following of the occupation. All people did not possess infinite patience, and if there was any form of treatment, medicinal, chemical, or electrical, which would get such cases well in a reasonable time, it was important to know it.

Mr. A. L. WHITEHEAD asked whether one could reasonably hold out hopes of relief from the tinnitus, which was often a serious discomfort. In the President's case tinnitus was unaltered, as also in two of Mr. Jones's cases. His own experience was that one could not hold out hopes of stopping tinnitus by opening the labyrinth.

Mr. MACLEOD YEARSLEY asked what was the condition of the patient afterwards. He had twice operated for severe vertigo. One of the cases he published in the *Lancet*¹ three years ago, and an account of the other was about to appear in the same journal. The first case was that of a clergyman, who was practically stone deaf in both ears, and had very severe tinnitus, on account of which he was beginning to threaten suicide. He also had severe vertigo, which quite incapacitated him. He (the speaker) destroyed completely the vestibular apparatus on the left side, as well as the cochlea. There had been no vertigo or tinnitus since, but he complained that he could not find his way in the dark. If he got out of bed in the dark he lost his bearings, collapsed on the floor and had to wait until morning, or until his cries for help brought some one with a light. On one occasion he turned out his study lamp

¹ *Lancet*, 1908, ii, p. 871.

before leaving his study and was completely lost; he could not even find his way to the bell. That symptom was now gradually getting better. The second case had normal hearing on the opposite side and suffered from incapacitating vertigo. The patient was now married and in the North of England. In reply to a letter asking as to her condition when in the dark, she said that was her greatest trouble. Although she might know the way was straight in front of her she could not imagine a clear space round her, and she felt lost and did not know what to do. In consequence of these cases he recently made inquiries among certain congenitally deaf boys, whose vestibular apparatus apparently did not function, as nothing could make them giddy, and they did not respond either to caloric or turntable tests. They had no trouble whatever in finding their way in the dark. The question occurred to him whether, in these congenital deaf cases, the muscular sense took the place of the vestibular sense, and whether in the adults on whom he had operated the muscular sense had had no opportunity as yet of adapting itself to the altered circumstances.

Dr. H. J. DAVIS thought that if there were disease in both ears nothing should be done, especially if the patient was old, as it was difficult to say in which ear the vertigo originated. That day he saw at the hospital an old man, aged 72, who was quite incapacitated. He was deaf in both ears, and had intense vertigo and giddiness. He insisted on something being done; in fact that afternoon he said if something were not done for him he would shoot himself. To do a crippling operation on both ears for a man at that age seemed to him out of the question. They were most pitiful cases.

Mr. SYDNEY SCOTT confirmed the views expressed by Mr. West, that few patients with vertigo should be operated upon. He had only operated on three cases of non-suppurative labyrinthine vertigo. He would give his experiences on some future occasion. It was curious that tinnitus so often persisted, even though the whole of the cochlea was destroyed.

Mr. C. E. WEST wished to correct in one particular the remarks he had made, as he had had one case, that of a woman, the whole of whose labyrinth he extirpated. She became maniacal from shock and giddiness, but finally got well.

Mr. JENKINS, in answer to Mr. West, supported Mr. West's caution with regard to operating in cases of vertigo, but if a comparatively slight operation would relieve the patient there seemed no reason why it should not be done. In answer to Mr. Lake he held that there might be an increase of labyrinthine pressure without increase of fluid.

Mr. HUGH JONES agreed as to the caution required in deciding to do an operation such as that under discussion, so that it was necessary to justify what he had done. In his second case he did all he could to avoid operation, trying to persuade the patient not to have anything done, and sending him a long letter setting forth all the dangers, including the chance of the facial nerve being injured. The patient, nevertheless, insisted on the operation being

performed. Since the operation the patient had been able to follow his occupation. In the last case he confessed to some doubt as to whether the operation ought to have been done or not, not because of the result, but because he thought the patient might possibly have recovered with ordinary treatment. But he believed two or three years or even longer were required before a patient was entirely free from attacks. He explained all the risks, but as she was a young working woman with a family, was having attacks twice a day, and had been for six months, he told her that two or three years' treatment might be compressed into a few weeks by operation. It was yet too soon to say what the ultimate result would be, but she was very much relieved. The first day he saw her after the operation she said the noise had entirely gone, and that she was much relieved. With regard to the first case, the man had been having attacks for ten years, and as he could not do his work he insisted on having something done. During the last fortnight he had refused to operate on two cases of the kind, in one because the patient was aged 65. The other was a man aged 35, in active business, whom he told to be content with ordinary treatment, which would probably get him well in two or three years.¹ As to the cure of tinnitus, he thought something would depend on the extent of the operation—operation on the semicircular canal alone seemed insufficient.

The PRESIDENT (Dr. W. Milligan) said the Section might take it for granted that Mr. Jones, Mr. Jenkins and himself had taken every possible means, general and local, before resorting to operation, for they realized the risks and the severity of the operation even when done with the utmost care. Still, there were cases which orthodox treatment did not benefit. He did not think that he had done more than eight of these operations altogether, an infinitesimal number compared with the number of cases he had seen. In some of the cases he had operated upon, medical treatment had been tried for years. In the case recorded treatment had been carried on for five years continuously by a very careful and intelligent general practitioner. With one exception, all his cases had been hospital patients, who otherwise were in good health, but who were compelled to make a living, and could not do so when they had to stand on walls, ladders, &c. With those precautions he did not think any critic, however severe, would take up the attitude that an operation should not be performed, even though risky. Immediately following the operation in the case recorded there was considerable shock, but it was of short duration, and then the patient recovered quickly. In none of his cases had the tinnitus been entirely relieved. He did not know how to diagnose tinnitus peripherally produced from that of central origin, and until that was possible one could not expect definitely to cure the condition. But the vertiginous symptoms were cured, and the patient was enabled to follow his occupation once more. The point mentioned by Mr. Yearsley was new to him, but he would be careful to find out about it; the apparent loss of the sense of space in the dark was very interesting.

¹ Two weeks after this was written, two severe attacks having occurred, superior vestibulotomy was performed with success. Tympanum not entered.

Notes of a very severe Case of Streptococcal Infection of both Ears, &c.

By GEORGE N. BIGGS, B.S.

I WAS called to see E. C., who gave the following history: On Saturday he noticed that he had a slight cold; on Sunday, at mid-day, both ears became slightly painful, the pain rapidly increased, and on Monday morning, when I saw him, he was looking very ill. Temperature, 104° F.; pulse, 110 and regular. Very severe frontal headache and vertigo. No nystagmus. On examination both tympanic membranes were found to be bulging and dark blue in colour; no mastoid tenderness, &c. Both tympanic membranes were incised and a culture taken, in order that a vaccine might be prepared. By midnight his temperature had fallen to normal.

On Tuesday, at 4 a.m., his temperature began to rise again, and when I saw him at 9 a.m. there was marked tenderness over the right mastoid, and severe right-sided headache; temperature, 103° F.; no other symptoms. His right mastoid was therefore opened, and the cells and antrum were found to be filled with the same sanious fluid that had escaped when the tympanic membranes were incised on the previous day. No pus was present. He was given an injection of polyvalent serum, as the autogenous vaccine was not yet ready.

After the operation his temperature fell to normal, but at about 5 the next morning it again began to rise, the left ear became very painful, and when seen at 9 a.m. there was marked tenderness over the left mastoid, severe headache, and temperature 102.2° F. His left mastoid was therefore opened, and although the cells contained sanious fluid, the antrum contained some pus, showing that he was beginning to react locally to the infection. He was given an injection of autogenous vaccine, which was now ready, the organism having proved on examination to be the streptococcus in pure culture.

Although very ill he improved slightly during the next three days, but on the fourth day his temperature rose to 103° F., the headache returned but was now frontal and very severe; at the same time he complained of pain in the throat and nose, and on examination both sides of the septum, the inferior and middle turbinal bones, the posterior wall of the pharynx, the tonsils, palate, and pillars of the fauces, were

seen to be extensively ulcerated. A culture was taken from the nose and throat in order that if a fresh organism was proved to be present a fresh vaccine could be prepared. The streptococcus was, however, again proved to be present in pure culture.

With the usual local treatment, and injections of vaccine at intervals, the condition fortunately subsided, but at one time I feared that the accessory sinuses of the nose would become involved, and necessitate further operative interference.

The patient fortunately made an uneventful though slow recovery; and the hearing, except for the loss of a few seconds, by air conduction to the C forks from 3C (16) to C₄ (2045), is practically normal.

Case of Thrombosis of the Right Lateral and of the Longitudinal Sinus.

By P. WATSON-WILLIAMS, M.D.

H. J., MALE, aged 37. Patient was admitted on November 27, 1911, to the medical wards of the Bristol Royal Infirmary, under Dr. Edgeworth, who kindly referred him to me on account of a purulent discharge from the right ear for three weeks, and to which he had been subject on and off for five years. He was intensely cyanosed, but Dr. Edgeworth could find no cause in the patient's condition for such a remarkable cyanosis, his heart, lungs and abdominal viscera being fairly normal. He had complained of severe frontal headaches before admission.

Blood count: Red cells, 3,810,000; leucocytes, 21,477; polymorpho-nuclears, 63·5 per cent.; hæmoglobin, 100 per cent.; small lymphocytes, 29 per cent.; large lymphocytes, 11 per cent.; transitionals, 1·5 per cent.; myelocytes, 0·5 per cent.

The temperature was fluctuating between 97° F. and 101° to 102° F., but there was a complete absence of tenderness or pain over the mastoid area. The optic disks were normal. It was felt at first that there was insufficient evidence of the febrile temperature being due to the ear condition, but as the symptoms persisted without explanation of the cyanosis, a radical mastoid operation was performed on November 29. The mastoid was infantile in type, and there was no softened area of the walls of the cavity operated on leading in the direction of the lateral

sinus or middle fossa. Subsequently it was ascertained that the patient had taken twenty "Daisy" powders before admission, the cyanosis being probably due to acetanilide poisoning.

The operation relieved the patient, but the febrile temperature persisted. A consultation with the surgeons of the Royal Infirmary was held, with a view to exposing the lateral sinus and ligaturing the jugular vein, but as there seemed a total absence of any evidence pointing to lateral sinus thrombosis, apart from the persistent temperature, the patient feeling very comfortable and being bright, and cerebration normally quick, it was decided to defer further operative interference.

December 7: Temperature rose to 104° F., and it was determined to explore. Before the operation was begun, and while being anaesthetized, the patient became nearly asphyxiated, tracheotomy being necessary. The lateral sinus was exposed, being separated from the mastoid antral cavity by a thick layer of hard bone. A peri-sinus abscess was found, and the sinus thrombosed. The sinus was opened up backwards nearly to the torcula, and forwards to the bulb; the internal jugular vein was ligatured above the common facial. No thrombus was found in the vein as far as it was exposed, but it was impossible to remove the clot sufficiently to wash out the vein above through the sinus. Cultures from the peri-sinus yielded Gram-positive streptococci and staphylococci.

The patient felt remarkably well the next few days, but the temperature remained above 102° F. Up to December 19 he was cheerful and bright, but after that he became mentally dull, and became rapidly weaker, dying on December 21.

At the autopsy the sinus thrombus occupied the whole of the longitudinal sinus, extended from the torcula a short way into the left lateral sinus. A leptomeningitis of the upper half of the cerebral hemispheres, which appeared to have been the cause of death, had evidently been set up by infection from the longitudinal sinus. The transverse, petrosal and cavernous sinuses had apparently escaped.

The remarkable features in this case were the absence of symptoms pointing definitely to lateral sinus thrombosis; although it was very extensive, the fact that this thrombosis extended back to the torcula and into the longitudinal sinus, without extending well down the internal jugular; and the remarkable absence of mental symptoms, despite the very extensive thrombosis of the intracranial sinuses.

Case of Peri-sinus Abscess and ? Lateral Sinus Thrombosis.

By P. WATSON-WILLIAMS, M.D.

H. H., BOY, aged 12, attended the Outpatient Clinic at the Bristol Royal Infirmary on March 9, 1911, complaining of some pain over the left mastoid region, well-marked vertigo, tendency to fall from right to left, and objective clockwise vertigo. Lately and vomited. There was a history of purulent discharge from the left ear since infancy, and from the right ear for one year. There was a large perforation in the right membrane, and the drum of the left ear had almost disappeared. Spontaneous nystagmus to left; caloric reaction delayed 90 seconds right and left. Fistel symptom not present. The temperature was normal, and the boy in fair health. Improved with local treatment, and went out under observation.

On December 14 he complained of severe headache, persistent vomiting, and tenderness behind the ear; vertigo increasing; optic disks showed fullness of vessels; no neuritis. That night the boy's temperature rose to 102° F., and an immediate operation was performed. On stripping the periosteum from the mastoid, pus welled up through the aperture of the emissary vein. The mastoid antrum was unusually large, extending $\frac{7}{8}$ in. backwards from Henle's spine, full of pus and cholesteatomatous contents. The lateral sinus was exposed; about $\frac{1}{2}$ dr. of pus escaping from the peri-sinus abscess. The sinus was not opened but it did not pulsate. There was no evidence of thrombosis in the jugular vein. The culture from pus yielded *Streptococcus brevis*, Gram-positive.

The patient recovered without any notable feature.

Case of Lateral Sinus Thrombosis.

By P. WATSON-WILLIAMS, M.D.

T. R., MALE, aged 24, was admitted to the Bristol Royal Infirmary on November 13, 1911, with a history of pain in the right ear for ten days, headache and rigors. Temperature, 102° to 103° F. He denied any previous ear trouble, but the right meatus externus was occupied by a

large aural polypus. On November 24 a radical mastoid operation was performed, and the large mastoid antrum was full of pus. A sinus leading to the lateral sinus—a peri-sinus abscess containing much pus—was evacuated; the wall of the sinus was thickened, but the sinus pulsated. After disinfection of the operation area by free application of spirit lotion containing $\frac{1}{1000}$ perchloride of mercury, a hypodermic needle was inserted and some clot withdrawn, blocking the needle. A second puncture was made, more deeply entering the sinus, and the blood withdrawn submitted to culture. The operation was completed without ligaturing the jugular or opening the sinus. From the day of the operation to his discharge from hospital on December 12 the temperature remained below normal except for two days, when it touched 98.6° F. His recovery was uneventful.

The culture of the blood drawn from the lateral sinus yielded Gram-positive staphylococci with a few Gram-positive streptococci, while the pus from the mastoid antrum contained staphylococci, Gram-positive and Gram-negative, but no streptococci.

Remarks.—The patient had a peri-sinus abscess and a mural clot in the sinus; but though the blood of the sinus was proved to contain staphylococci and streptococci, the patient recovered without untoward symptoms and without ligation of the jugular vein, &c.

DISCUSSION.

Mr. HUGH JONES mentioned a case in which the thrombus extended round to the opposite lateral sinus, and was associated with a temporo-sphenoidal abscess, which was evidently the direct result of contiguity of the opposite sinus with the brain. There were no definite signs at all, and the thrombosis was only discovered because there was an external abscess over the mastoid, and the temporo-sphenoidal abscess post mortem.

Mr. SYDNEY SCOTT was reminded by Dr. Watson-Williams's first case of a similar one, upon whom Mr. West and he had operated for lateral sinus thrombosis some years ago. The patient was a boy who was intensely cyanosed, and they were very much puzzled to know the reason, for the heart, lungs and heart's blood were normal; furthermore the cause of death after the operation was never clearly explained. He now suggested to Mr. West that this patient may have been dosed with so-called "Daisy" or similar powders previous to the operation, as in Dr. Watson-Williams's case.

Mr. WEST said Mr. Scott's suggestion was a happy one to account for the sequel in a case which had always puzzled him.

Mr. ROBERT WOODS asked whether in the first of these cases there was evidence of œdema over the forehead. In the only case of thrombosis of the superior longitudinal sinus which he had seen that sign was not very marked, but it was quite evident on being searched for.

Dr. WATSON-WILLIAMS, in reply, said he did not know much about "Daisy powders," but he was told that they were largely acetanilid. The striking feature of the first case was the very marked cyanosis, which led the physician to search for intrathoracic conditions as the cause, but there was nothing to account for it from the internal medicine point of view. A specimen of the blood was taken because it was thought to be a case in which there might be methæmoglobin as a result of the sulphur bodies in the blood; but it was absent. No vaccine treatment was employed.

Mr. ROBERT WOODS, in reply to Dr. Watson-Williams, said the case was treated by ligature of the internal jugular vein on the right side. It was assumed that the superior longitudinal sinus pursued the usual course and opened into the right lateral sinus. The lateral sinus was opened behind to find out if the thrombus extended that distance, but it did not. There was a perfectly good recovery.

A Case of Operation for Extreme Deafness and Tinnitus due to Chronic Adhesive Catarrh of the Middle Ear (Tympanoplasty).

By HAROLD A. KISCH, F.R.C.S.

A WOMAN, aged 43, with a history of extreme deafness of the right ear of at least ten years' duration and of increasing deafness of the left ear. Tinnitus and fullness of the head were marked symptoms, but there was no paracusis Willisii. She had been treated unsuccessfully for several years by the usual methods. Eustachian catheterization only improved the hearing slightly for a very short time. The tympanic membrane on the right presented a similar but rather more retracted appearance to that now seen on the left side.

On October 31, 1911, a radical mastoid operation, followed by immediate skin-grafting, was performed on the right side. The tympanic membrane, the malleus, incus, and all the mucous membrane and tissue of the middle ear were removed. The stapes was not interfered with. A broad adhesion was found passing from the drum to the promontory, and the mucous membrane was thickened. The ossicles

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were not ankylosed. After-treatment by vibratory massage to the ear and petrous bone has been systematically carried out.

The hearing results are as follows, but she tends to vary slightly from day to day:—

Tuning fork			Before (Oct. 30, 1911)			After (Feb. 1, 1912)
C. 128	- 145	- 70
C. 256	- 44	- 20

Before operation she was only able to hear the loudest shout close to the ear and a whisper not at all. She now hears the voice at 13 ft. and a whisper at 8 ft. The tinnitus and fullness in the head from which she suffered have also much improved.

A similar operation, with the addition that a foramen was made in the promontory, has been done on a boy. The graft over the foramen was planted on the endosteum lining the promontory. A great increase in hearing has resulted. This case will be shown at a subsequent meeting.

DISCUSSION.

Dr. URBAN PRITCHARD said that this class of case came under the category of what Professor Politzer thought might be advantageously treated by operation. It was a fibrosis, not oto-sclerosis—i.e., one in which there were fibrous bands across the tympanum, probably not many in the pit containing the stapes, or Mr. Kisch would not have succeeded. He always thought that now and then one would get a case in which an operation such as this would produce considerable benefit. But there would not be many cases of the kind.

Mr. MACLEOD YEARSLEY suggested that the case might be shown in another year to see if the result was maintained.

Dr. WATSON-WILLIAMS believed Mr. Kisch would have had as good a result in regard to hearing, and possibly a better eventual result, if he had simply avoided curettage of the mucous membrane in the neighbourhood of the stapedo-vestibular joint, when he performed the radical mastoid operation. He supposed that the patient was hearing by means of the stapedo-vestibular joint, and it was unnecessary to destroy the mucous membrane of the inner wall of the middle ear. As good results were obtained after mastoid operations in which the mucosa of the inner tympanic wall was preserved. He believed there would have been even better hearing in this case if skin-grafting had not been done.

Mr. WAGGETT asked whether Mr. Kisch included among the ordinary methods the use of the Lucae probe, which seemed now to be somewhat forgotten. One got remarkably good results with it in many cases where Eustachian massage was useless.

The PRESIDENT referred to some remarks made before the Otolological Society by Dr. Pritchard, in which he said: "A vague idea has struck me as to the possibility of making a new fenestra when the fenestra ovalis is rendered useless. Could we open the membrana tympani, drill a hole into the labyrinth and graft as it were a flap of the membrane over the hole, so as to form a membrane for the new artificial fenestra?"¹ He would have liked to have had more information as to the condition of the patient before operation, and the response to the tests now. He had himself done the operation two or three times, but he never got such a result as to make it worth while thinking of the operation as a routine measure. In this case the result seemed to be mainly due to the removal of the adhesion between the membrane and the inner wall of the middle ear. He agreed with Dr. Watson-Williams that if an operation of the kind were entertained it was better to leave the mucous membrane on the inner wall of the middle ear intact, because if it were removed it was almost impossible to know whether or not it would be reproduced in a sufficiently healthy condition afterwards; if not, it would spoil the effect of what might otherwise have been a good operation. But the idea of such an operation was good, and in very severe cases no harm could be done by the attempt. Mr. Kisch deserved congratulations on his result, which he did not think would have been so good if it had been limited to an ossiculectomy. He would be glad if Mr. Kisch would show the case again a year hence.

Mr. KISCH, in reply, said that originally he intended to show the case in six months' time, but the patient's hearing had been stationary for nearly a month. He would show the case again a year hence. He excluded otosclerosis as far as possible by means of the ordinary tests. He did not curette, but simply stripped the mucous membrane off with a narrow blunt separator, as he did not wish to damage the stapes. The idea of removing the mucous membrane and grafting was to obtain immediately a healed surface. Mucous membrane, exposed to the air, would undergo cicatricial changes, and probably cause fixation of the stapes. There was no difficulty in removing the mucous membrane, or in putting on the skin. He had done the same in two other cases, and although the time was short since the operations, they were showing the same results as in this woman. He had not had much success with Lucae's probe. His idea in applying vibratory massage was to stimulate the labyrinth. The patient had not heard with that ear for ten years, so that the labyrinth was probably, so to speak, out of gear. It was remarkable how she improved each time after the massage, and strychnine was also being administered. With regard to Dr. Pritchard's remarks, which were quoted by the President, he was not aware of these, but he had not claimed the idea as new, because he felt sure that it would be found that someone had suggested it before. He thought, however, there were several new features in his method.

¹ *Trans. Otol. Soc., U.K.*, 1906, vii, p. 62.

**Yankauer's New Speculum for the Direct Examination of the
Nasopharynx and Eustachian Tube.**

By P. MACLEOD YEARSLEY, F.R.C.S.

THE speculum consists of a tube of peculiar shape which is introduced into the nasopharynx and illuminated by the ordinary head-mirror. It acts as a palate lifter, and as the anterior wall of that part which lifts the palate is in a straight line with the posterior wall of the part which presses the mouth back, it enables the observer to bring into view the orifice of the Eustachian tube and part of its anterior wall.

Its introduction is accomplished by passing the beak under the soft palate, while the body of the tube lies across the tongue, and the proximal part of the instrument rests in the angle of the mouth, on the opposite side. The patient's head is held backwards as far as possible, and turned to an angle of 45° toward the side to be examined. The use of cocaine is necessary for the first few introductions, but patients learn to tolerate the speculum.

The first part which comes into view is the vault of the pharynx, then the fossa of Rosenmüller, the posterior lip of the tube, the orifice of the tube, and part of its anterior lip. To see the last two parts, an anæsthetic, local or general, seems necessary.

As the smaller orifice of the tube measures 1 in. by $\frac{5}{8}$ in., the view obtained is good and it is possible to use instruments, such as forceps or curettes, through it, to make applications to the Eustachian tube, or to inflate the ear with a straight catheter. I have already found the speculum valuable, and I am using it in combination with the Holmes's electric nasopharyngoscope that I showed here the meeting before last. The latter gives so clear a view of the nasopharynx with a little practice that I have been able to make drawings of the conditions seen, and some of these I hope to show to the Section early next session. For treatment, however, the Yankauer speculum is much more convenient, as it enables one to manipulate by direct vision.

DISCUSSION.

Dr. H. J. DAVIS said those who were in Berlin in September might have seen a demonstration given at the Charité of the examination of the Eustachian tube by Dr. Gyergyai, of Budapest. It was done with a

Brünings's handle lamp with a very short tube, under cocaine anæsthesia, the patient's head being well over the table in the examiner's lap. The finger was passed behind the palate first, and the tube passed beside it and the light turned on, and the Eustachian tubes could be easily seen as well as the entire post-nasal space. It gave a stronger light than Yankauer's, and one could easily see whether adenoids were present or not. The head of the patient was placed right over the end of the table as in Rose's position for the adenoid operation, and the examiner sat on a stool at the head of the patient and held the extended and overhanging head between his knees. He had tried it since with a small Brünings's tracheal spatula, and obtained a good view. The tubes designed for this examination were of six different sizes and could be obtained at Deteil's in Berlin.

The PRESIDENT remarked that in order to intensify the view through such a speculum, Chevalier Jackson's method might be adopted of having a very small lamp at the end of the speculum.

Tuberculous Disease of the Temporal Bone in a Boy, aged $7\frac{1}{2}$.

By W. H. KELSON, M.D.

FIRST operated on at the age of $6\frac{1}{2}$ months. Tubercle bacilli found in the discharge and tissues. Quite well for four years, then recurrence and operation. Again well apparently for a year, then recurrence and operation. Tuberculin injections tried, but apparently no benefit.

DISCUSSION.

The PRESIDENT asked whether tubercle bacilli were found in the soft tissues or in the bony tissues. In his experience the best place to find bacilli was just where the disease invaded the bone. He had had great difficulty in finding them in the discharge, and only occasionally had he found them in granulation tissue. But he had found the bacilli many times in the advancing edge of the disease. Considering the boy's condition, he would like to know whether Dr. Kelson intended to perform a plastic operation to close the fistula behind the ear. Also, what doses of tuberculin were given, and how many. He had himself had one or two cases which reacted well to tuberculin injections, controlled by the opsonic index. In one case repeated operation having failed to eradicate the bone disease further operations combined with tuberculin injections resulted in complete healing with the exception of facial paralysis and loss of hearing on that side.

Mr. A. L. WHITEHEAD asked whether Dr. Kelson grafted in this case. He had followed one case for years, a girl who had recurrence four times, the

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intervals having varied between nine months and two years. She had no other manifestation of tuberculosis. Bacilli were not demonstrated, but she had tuberculous tissue, and giant cells. In his opinion grafting was not desirable in tuberculous cases.

Dr. KELSON, in reply, said tubercle bacilli were found in the discharge and in some granulation tissue which contained a spicule of bone. The tuberculin used was Burroughs Wellcome & Co.'s 'tabloids,' 100000 mg. of the new tuberculin, which was injected every week for some months, but there was no apparent result. He did not believe in closing the cavity until healing was complete; there were still some pockets due to the breaking down. Mr. Whitehead's case in which there was difficulty in getting it to heal proved that it was a mistake to do a plastic operation until the case appeared to be cured. He had not tried the Finsen light or anything of that sort. Grafting was done at the second operation. Again it did well for two years, and then reappeared.

Solid Symmetrical Œdema of both Auricles in a Woman, aged 36; Twelve Months' Duration.

By H. J. DAVIS, M.B.

BOTH pinnae have been in the condition observed for twelve months. The auricles are red, swollen, and pit on pressure; the meatus is swollen and there is a discharge from both canals, but only the left membrane is perforated; the right is normal.

The case was exhibited by my colleague, Dr. Abraham, at the Dermatological Section, but no diagnosis was made. The case is not a perichondritis, though it looks like it; Wassermann reaction negative; Von Pirquet reaction negative; physical signs of old adhesions in the chest and old interstitial keratitis.

The photographs of the auricles were taken by Dr. Morton.

DISCUSSION.

Mr. ROBERT WOODS said the case seemed to be analogous to elephantiasis, which one saw more often in the old days, from repeated attacks of erysipelas, where in consequence of repeated inflammations the subcutaneous tissue underwent enormous hypertrophy. He thought in this case the hypertrophy was due to repeated attacks of acute inflammation proceeding from an eczema of the external meatus, and that repeated attacks of acute inflammation produced the hypertrophy now seen.

Mr. A. L. WHITEHEAD regarded the case as one of chronic inflammatory condition due to repeated infection, and he suggested that an autogenous vaccine should be prepared from the discharge and inoculated.

The PRESIDENT also thought it was the result of repeated infection. It seemed to be too dense for elephantiasis, and treating with an autogenous vaccine appeared to him to be a good idea.

Dr. DAVIS, in reply, said that when he first saw the case he thought it was due to infection from the aural discharge, but dermatologists who saw it would not accept that idea, but discussed elephantiasis, tuberculosis, syphilis,



Right ear.



Left ear.

Solid symmetrical oedema of both auricles. The entire pinna is involved.

leprosy, and other diseases. It was thought to be tuberculous, but the culture from the skin was sterile. There was otorrhœa now on the left side alone. The patient had the physical signs of old phthisis in the chest, and she showed interstitial keratitis with central corneal opacities. He thought she was syphilitic, but the Wassermann reaction was negative. She had been no better after having the ear syringed. He would have a vaccine made and injected.

[March 7: Attempts have been made to obtain a vaccine, but the meatal discharge having ceased this failed; the ears remain in the same condition.—H. J. D.]

Result of Perichondritis of Auricle in a Boy, aged 17.

By H. J. DAVIS, M.B.

IN May, 1911, a radical mastoid operation was performed for long-standing otorrhœa; wound healed in a week. A fortnight later perichondritis supervened; incisions were made on four occasions under gas before the inflammation subsided. Shrivelling of the affected area resulted, and the upper part of the pinna dropped away from the side of



Perichondritis of auricle. The upper half of the pinna is alone affected.

the head. Two months ago a plastic operation was performed in order to reduce this deformity, and the ear is now in contact with the head.

If the photograph of the ear is compared with that of the auricles of the woman just mentioned, it will be noticed that the upper half of the pinna is alone affected, and this is what happens in perichondritis; whereas in the previous case the entire pinna is seen to be involved. The exhibitor some years ago exhibited a man in whom this had resulted on both sides.¹

Dr. Jansen, to whom the exhibitor had mentioned these matters lately in Berlin, said that the only thing to do in these cases was to dissect out the cartilage at once to arrest the process, and this is what he recommended.

¹ *Proceedings*, 1910, iii, p. 71.

Otological Section.

March 15, 1912.

Dr. W. MILLIGAN, President of the Section, in the Chair.

The Value and Significance of Hearing Tests.

Addresses Introductory to a Discussion on the Subject.

(I) By THOMAS BARR, M.D.

It has been arranged between Mr. Sydney Scott and myself that I should take up the tests employed to determine the state of the bone-conduction of sound and its relation to air-conduction.

The value, as a means of differential diagnosis in diseases of the ear, of applying tests to determine the relations between bone-conduction and air-conduction of sound, must be a subject of great interest to the modern otologist. The object of these tests being to differentiate disease of the sound-conducting structures from that of the nerve structures, it should be of almost equal interest to the physician.

At this point, may I ask, why should we regard the conducting apparatus as simply extending to and including the fenestral structures? This appears to me to be an arbitrary division. It is more correct, I think, to regard the conducting structures as extending to the cochlear nerve terminals. There are pathological conditions in the interior of the labyrinth which do not directly affect the nerve perception, but which interfere with structures which are to all intents and purposes conducting media. That intra-labyrinthine disease does not necessarily involve the nerve apparatus is perhaps not sufficiently taken account of in considering tests by bone- and air-conduction.

Our subject has been the theme of very many contributions to otology, and upon it great industry, ability, and learning have been expended, especially by our German and Austrian confrères. Very divergent opinions have been held as to the comparative value and significance of the various tests employed. Some authorities are doubtful as to whether they materially facilitate our diagnosis. Of course we all admit that they have their limitations, and that in their application there are difficulties, apparent contradictions and possible fallacies, but withal they are still, I believe, capable of yielding valuable information and settling a doubtful diagnosis. I shall first refer to a few of the limitations and difficulties.

There is the limitation of age. We all know that, owing to changes in the cranial bones and in the auditory nerve, the intensity of bone-conduction diminishes in advancing years, and therefore these tests are largely inapplicable in patients over 55 years. This excludes a large number of patients. From my recorded testings, bone-conduction predominates over air-conduction in about twice as many patients under 30 years of age as over 50 years. I have found, however, that Weber's test gives reliable results in elderly people.

There is the difficulty of getting accurate replies, especially from patients who are uneducated and of only moderate intelligence. For example, we cannot always trust to the accuracy of a patient's statement as to the exact moment at which a sounding tuning fork ceases to be heard, either by bone-conduction or by air-conduction. This is sometimes difficult even in the case of a quite observant and intelligent patient. We have only to try it upon ourselves to appreciate the difficulty.

Then there is the time and patience required, which some of us may not possess, to carry out a satisfactory examination and to make the necessary verifications. We all know how absolutely necessary it is that these testings should have sufficient time given to them, and some have said in their haste that the results are hardly commensurate with the time and trouble expended. Certainly as one occasionally sees them carried out in noisy dispensary practice, hurriedly and perfunctorily, one feels that but little reliance can be placed upon the results.

There is the well-known difficulty, in connexion with Weber's test, of getting the patient to rid himself of the belief that he must necessarily hear the sound of the tuning fork more strongly on the normal or better side. While in some patients we get a prompt and correct reply, though it may be opposed to his preconceptions of what should be, in others

much explanation and patience are necessary to get him to understand that he *may* hear the tuning fork better on the affected side; but as a rule we ultimately get at the truth.

There is the difficulty of one test apparently contradicting or conflicting with another, such as Weber's test conflicting with Rinne's, or a low tuning fork giving a different result from a higher one.

Once more we have the undoubted experience of all observers that objective examination may show clear signs of middle-ear disease, and yet Rinne's test may be positive, or, on the other hand, though more seldom, there may be indubitable proof of nerve disease, while Rinne's test yields a negative result.

The tests most commonly employed in everyday practice are Weber's, Schwabach's, and Rinne's; less commonly Gellé's, Bing's, and Bárány's.

I shall not take up your time with the watch test, to which the older otologists pretty much limited themselves in testing bone-conduction, and which is not to be entirely despised. It is no doubt a handy test, only suitable, however, when the deafness is very marked, otherwise it is heard by air-conduction, as well as bone-conduction, which vitiates the result. It is usually advised that the ears be closed during the testing; this, however, by increasing the bone-conduction, would also vitiate the result. It may be said that if a moderately low ticking watch is perceived by bone-conduction, where there is marked speech deafness, it is a favourable indication as to the state of the nerve structures. The opposite need not, however, be regarded in itself as necessarily unfavourable.

In carrying out these tests, however, the tuning fork is now universally employed. As a routine I am in the habit of limiting myself to two tuning forks, a low one (C, 128 vs.) and a higher one (C¹, 256 vs.), the over-tones being abolished by means of suitable clamps. The end of the handle should be flat, so as to rest evenly on the bone; the handle should not be in contact with the auricle. The pressure on the bone should be uniform and not too strong—strong pressure will prolong the sound as compared with light pressure. The fork should not be sounded too loudly, so as to avoid wearying the auditory nerve by the too prolonged excitation.

WEBER'S TEST.

This is probably the oldest method of testing by bone-conduction, and must be regarded as a test of undoubted value in unilateral deafness, or when one side is markedly worse than the other. Some authorities, such as Politzer, regard it as the most reliable of all the tests. If the low tuning fork, applied to the middle line of the head (I prefer the chin), is unhesitatingly stated by the patient to be heard more loudly, or it may be exclusively, resonating on the deaf side, there are, I think, very few exceptions to the rule that there is some form of obstruction or disease in the sound-conducting apparatus. There may, however, be a co-existent nerve defect, so that Rinne's test may be at the same time positive. For example, exudative conditions, without perforation, almost always show, by Weber's test, lateralization to the affected side, while they may, and fairly often do, give a positive result by Rinne. I found in thirteen of such cases Weber was referred to the deafer ear in every case, while in four of them Rinne was positive. So in twenty-five cases of ceruminous collection, Weber's test was referred to the deafer side in every one, where this test was applicable, while in twelve of them the result of Rinne was positive.

If the contrary effect be found, the sound being referred to the non- or less affected ear, we have good ground for excluding an obstruction in the sound-conducting media and for suspecting a nerve affection, provided we take sufficient time and trouble to ensure that the patient's statement is to be accepted. If this contradicts Rinne's test, I prefer to accept Weber, as in the following case: An intelligent patient was successfully operated upon for labyrinthine disease. In one ear the hearing was such that only loudly spoken words into the concha were understood. The opposite ear was perfectly normal; with Weber's test, repeatedly verified, there was lateralization to the *normal* side. Rinne's test, however, with both tuning forks, yielded a distinctly negative result on the affected side. I accepted Weber's test as the true guide, the negative Rinne being probably due to bone-conduction in the normal ear.

In bilateral deafness, the one ear, however, being less affected than the other, the patient is usually unable to speak so positively as in purely unilateral; he has difficulty in immediately deciding on which side he hears the fork better, and may end by saying it is the same on both sides. Even in such cases, however, if an intelligent patient is

confident that the tuning fork resonates in the *better* ear, a nerve affection is to be suspected, and this is strengthened if high and low tuning forks agree.

SCHWABACH'S TEST.

This probably is the simplest of the tests and often yields valuable information. We note the time during which a vibrating tuning fork is heard, when applied to the cranial bones, such as the vertex or base of the mastoid, on a person having defective hearing, and then compare it with one who has normal hearing, both being approximately the same age. This last condition is very important, as were we to compare the bone-conduction of an elderly person with one much younger the results would be quite unreliable.

The longer the tuning fork is perceived by the bone, in comparison with a normally hearing person, the more certainly may it be inferred that the sound-conducting structures are involved and that we may exclude impairment of the nerve structures; a comparatively short duration is not so conclusive in itself, but suggests nerve impairment. In my experience defective bone-conduction in young people, who have pronounced speech deafness, has always a sinister meaning.

As opposed to Weber's test, Schwabach's is most suitable in *bilateral* deafness. In unilateral deafness, or when one ear is very much better than the other, the results are usually rendered unreliable owing to the difficulty of eliminating the effect of the good or better ear in increasing the sound; if, however, there is a weak bone-conduction it is significant. Occluding the good ear would confuse matters, as, unlike what takes place by air-conduction, it would intensify the sound.

RINNE'S TEST.

This test was introduced by Rinne in 1855, but received little attention till Lucae resuscitated it in 1880. In Rinne's test I employ both tuning forks; the low fork sounds longer by bone and shorter by air-conduction than the higher one. This is no doubt accounted for by the fact that, in disease of the sound-conducting structures, low notes are heard badly by air-conduction, and therefore a negative result is more likely with the low fork than with the high one. I feel more assured, however, if the high fork agrees with the lower one.

In drawing our conclusion from Rinne's test, we must keep in mind

that the tone should be heard twice as long by air-conduction as by bone-conduction, and that therefore a negative result means much more than at first sight appears; so likewise a *shortened* positive should be considered in the light of the normal condition.

It may be broadly stated that in negative Rinne, the longer the osseous hearing continues after the aerial hearing has ceased, the more likely is the diagnosis that of disease of the conducting media; so in positive Rinne the longer the aerial hearing continues after the osseous hearing has ceased, the more likely may the case be regarded as one of nerve deafness. Again, it may be said that, if there is a prolonged negative result with the *higher* tuning fork, the greater is the likelihood of an affection of the conducting media, while, on the other hand, if there be a prolonged positive result with the *lower* tuning fork, the diagnosis of a nerve affection is strengthened. We have, therefore, not only to determine the fact of increased bone-conduction or of increased air-conduction, but we have to determine the *amount* of increase or decrease, and this has to be done by careful measurement with the watch, recorded in seconds. When we consider that aerial hearing should be twice as prolonged as osseous, equality—that is, when it is neither positive nor negative—is in favour of disease of the conducting structures. Of course in the routine of daily work accurate measurements with the watch cannot be carried out in every case, but where exhaustive examination is required these are necessary.

The diagnostic importance of the negative result of Rinne's experiment, especially in its bearing upon the presence of fixation of the conducting structures, has been anatomically confirmed by post-mortem examination by Lucae, Politzer, Bezold, Hartmann and Siebenmann. Dr. Alfred Denker, in his "*Die Otosklerose*," has gathered together twenty-seven cases in which anatomico-pathological examination after death supplemented careful clinical observations during life. These cases yield important information, both macroscopic and microscopic, confirmatory of the value of Rinne's, Weber's and Schwabach's tests. Into this department, however, I cannot extend my observations.

Rinne's test, like Schwabach's, is generally unsuitable in purely unilateral cases, because if there be good hearing in one ear the bone-conduction of the healthy side cannot be excluded and preponderates over the remnants of air-conduction in the diseased ear, although it be a nerve affection. It is also unsuitable where the hearing is but slightly impaired, as in such a case there is likely to be a positive result, even in the disease of the conducting structures. Probably Lucae is correct

in saying that this test is only of diagnostic value when the hearing distance for whispering has decreased to one metre.

There is no doubt that Rinne is not infrequently found to be positive when, from objective examination or the results of other tests, we should expect it to be negative. This is, I believe, often due to the co-existence of nerve impairment with disease of the conducting structures. There may be a concomitant nerve affection; but we must also remember that many of the conditions of civilized life tend to impair the nerve of hearing. For example, there is the great use of such medicines as quinine and the salicylates; and there is the frequent presence of specific disease. But probably the most common cause of nerve impairment is the frequency with which people work and live amidst noisy surroundings, in workshops, on the streets, and even at home; noises prevail in modern civilized communities as they have never done before. In these ways the exquisitely delicate nerve structures of the cochlea are frequently more or less permanently damaged. In my clinic at the Western Infirmary, Glasgow, many of the patients are riveters, boilermakers, engineers and others working amidst very noisy surroundings, in connexion with the great Clyde shipbuilding industry, which is carried on in the neighbourhood. We find in these patients, almost always, defective bone-conduction, and Rinne's test is positive even when there is also very evident external or middle ear disease. I examined the hearing of 100 boiler-makers, without selection, and in each man I also employed Rinne's test with a C tuning fork. Not one of them had normal hearing as tested by speech and the watch. In some the deafness was extreme. *They nearly all had very bad bone-conduction.* In 90 of the 100 Rinne's test yielded a very positive result, defective bone-conduction was shown by Schwabach's test in every one, while the watch applied to the cranial bones was only heard by thirteen men. It is interesting to observe, when such men come to the dispensary with aggravation of the deafness, owing frequently to a ceruminous obstruction or to a tympanic catarrh, how rarely we find a negative Rinne. I notice, however, that when the plug of cerumen or the tympanic catarrh is one-sided, Weber's test is usually lateralized to the affected side, although Rinne's test is positive.

It is remarkable how generally a *negative* result is found in purulent disease of the middle ear. Of 170 ears, representing all forms of ear disease, taken consecutively, tested by the low tuning fork, a negative result was found in 63 per cent. On the other hand, of the purulent

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cases alone, by which I mean cases with partial destruction of the tympanic membrane, both in the secreting and non-secreting stage, I found a remarkable preponderance of bone-conduction, there being a negative result in 98 per cent. This has been confirmed by further testing both with high and low forks. It compares with 43 per cent. of negative results in cases of chronic adhesive catarrh, and 52 per cent. in cases of ceruminous obstruction; in the latter, however, by Weber's test, the fork always resounded in the worst ear.

I observed in these purulent cases not only increased perception by bone-conduction, but also comparatively decreased perception of the tuning fork by air-conduction. Take, for example, two patients—one with chronic adhesive catarrh, the other with chronic purulent middle-ear inflammation. In the purulent case, hearing for speech and the watch was fairly good, while the tuning fork, by air-conduction, was heard very badly; in the case of adhesive catarrh, the hearing for speech and the watch was very poor (much worse than in the other), yet the tuning fork, by air-conduction, was heard twenty seconds longer. In these cases, therefore, the fork is heard badly by air-conduction, not merely in relation to the bone, but compared with air-conduction in an ear which may have equal or worse hearing for speech or the watch. We should, therefore, ascertain how much the air-conduction with the fork is reduced, in comparison with a normal ear, or with an ear whose hearing for speech is still more seriously impaired.

By *Gellé's test* we produce an artificial labyrinthine disturbance by condensing the air in the meatus, so that the foot-piece of the stapes shall press unduly upon the fluid of the labyrinth. This is an interesting but a troublesome test, the difficulty here being even greater than in the other tests of getting reliable information from the patient, especially as to the presence or absence of a temporary weakening of the tuning fork sound. In the more severe forms of deafness this test may be useful; even in these, however, a positive result is not constant. In the slighter forms of hearing defect it is untrustworthy. I have found Bárány's method, with a T-shaped rubber tube, an advantage in carrying out the test, as, by it, the condensation and rarefaction of the air in the meatus are more efficiently effected.

Bing's is a useful supplementary test. If after the fork, applied to the mastoid, has ceased to be heard, the sound returns when the meatus is stopped with the finger, we may infer, if supported by other tests, a nerve affection, otherwise it would strengthen the view of an affection of the conducting media.

Bárány's new tuning fork tests are described in a paper by the late E. Cresswell Baber,¹ probably the last contribution made to otology by our lamented friend. *Bárány* compares mastoid conduction with conduction through the cartilage of the auricle, with or without the help of an auscultation tube. Cartilaginous conduction seems to respond to tuning fork tests somewhat similarly to aerial conduction in Rinne's test. I can only speak from a very limited experience of *Bárány's* tests. Apparently in some of those cases where Rinne's test seems to conflict with Weber's, the former being positive when Weber's test shows lateralization to the affected ear, *Bárány's* test yields a negative result, thus supporting Weber and pointing to predominant disease of the conducting media. *Bárány* holds that his methods give a more reliable result than Rinne's. However, a much larger experience by many observers will be necessary before deciding as to whether they are superior to Rinne's test.

In reviewing these various tests, we have to remember that in practice we have to deal with mixed affections, so that there often exists in the one person simultaneous affections of the conducting structures and of the nerve structures, the affections of the one region (in its influence on the bone-conduction) tending to counterbalance, partially or wholly, that of the other region. While negative Rinne in a deaf person does not necessarily entirely exclude mischief in the nerve structures, but may simply indicate that there exists in the conducting structures a condition that is sufficient to more than counterbalance, in regard to the bone-conduction, the effects of the nerve disease; so a positive Rinne does not necessarily exclude disease of the conducting structures, but may simply mean that there exists in the nerve structures a condition which more than counterbalances the effects of the mischief in the conducting structures. In these mixed conditions, it is specially important not only to determine whether Rinne be positive or negative, but to find the extent of the positive or the extent of the negative, as measured in seconds.

We have to admit that these tests have their limitations, that each taken by itself may not be convincing, but this can be said in regard to most tests applied to determine the state of the function of an organ. Such tests have usually to be supplemented or strengthened by others. When Bezold's trio—Schwabach's, Weber's and Rinne's—agree, showing

¹ *Lancet*, 1910, i, p. 996.

that osseous hearing is in excess, we are on safe ground, the diagnosis admits of little doubt. In more doubtful cases qualitative testing by means of tuning forks and Galton's whistle will in many cases aid greatly in the diagnosis. Finally, we would properly and naturally consider all these tests, not only in relation to one another, but also in connexion with the symptoms, subjective and objective, of the patient, and such factors as the history, ætiology, and results of treatment. In these ways we shall generally be able to arrive at a fairly accurate diagnosis.

In conclusion, might I suggest that a reliable and simple formula for recording the results of hearing tests—both by air- and bone-conduction—is still a desideratum. The most recent authoritative formula, that presented by the International Otological Congress held in Budapest in 1909, has not, I think, the merit of simplicity. At least I found it a difficult bit of work to unravel it. We want a more simple method, one which can be easily followed and remembered, not only by the specialist, but by the physician or surgeon. Such a formula would be specially useful in the work of a general hospital, when we are called on to report cases in the wards, and when a post-mortem may be looming. We want a formula not only understandable by the specialists but also by the ordinary house surgeon and the visiting surgeon and physician. Could not this Section try its hand at this and appoint a committee to carry it out?

Allow me to thank the Council for the honour of being one of the openers of to-day's discussion. I am afraid I cannot pretend to have placed before you anything with which you are not already familiar. I can only hope to have offered you material, culled pretty much from my own clinical experience, which may help in eliciting profitable discussion. I shall leave the more abstruse problems of hearing to my colleague, Mr. Sydney Scott, who is so well qualified to deal with them in the true scientific spirit.

(II) By SYDNEY SCOTT, M.S.

A DISCUSSION on hearing tests presupposes a knowledge of the hearing tests in general use by otologists. The object of these tests is to deduce from the phenomena observed the physiological efficiency of the 'organ of hearing.' Certain phenomena in connexion with sound perception would indicate a normal physiological condition of the 'ear'; other phenomena would denote an abnormal physiological state. According to the complex of observed data we should be able to assign certain anatomical abnormalities to particular physiological defects. I propose to introduce for your deliberations certain fundamental principles. For instance, we know that sound requires the presence of matter for its transmission from the sound generator to the auditory nerves, without which no sensation of hearing is possible. The physical state of the matter, whether solid, liquid, or gaseous, is immaterial. The transmission of sound is due to the motion of each particle of the medium to and fro in the form of longitudinal waves which travel in the same direction as that in which the particles move. For the purposes of this discussion we shall submit the following hypothesis, which is founded on anatomical, physiological and clinical considerations.

The sensation of hearing is evoked by tactual stimuli set up by that form of oscillatory motion known as sound, which is communicated through the medium of the labyrinthine fluid to the membrana tectoria and the fibrillæ of the hair-cells in the organ of Corti. The impressions produced by such stimuli are conveyed from Corti's cells to the auditory centres in the brain by the afferent and projection fibres of the cochlear division of the eighth cranial nerve.

The form of oscillatory motion which is capable of producing sound stimulation is known as pendular or harmonic motion and is exemplified in solid bodies by the vibrations of a tuning fork, each limb of which swings to and fro in a manner which resembles that of a pendulum in motion. The double to-and-fro movement of a limb of the fork occupies a certain definite period expressed in time units which is constant for each fork; the range of displacement or excursion of oscillatory movement of any particle of the fork is called the amplitude of that particle and is measured in units of length. Given certain vibration-frequencies and certain amplitudes, a tuning fork when vibrating disperses its energy partly in overcoming the inertia of the

surrounding medium and partly in the conversion of internal friction into heat. When the fork is vibrating in air the particles of air vibrate in harmony with the fork, and provided the energy be sufficient, the waves of oscillation spread through the air and impinge upon some other form of matter, according to the density of which either reflects the waves, or is in turn set as a whole into corresponding states of vibration, the frequency and amplitude of which may be modified by physical conditions. The waves which reach the normal ear impinge upon the membrana tympani and auditory ossicles and walls of the

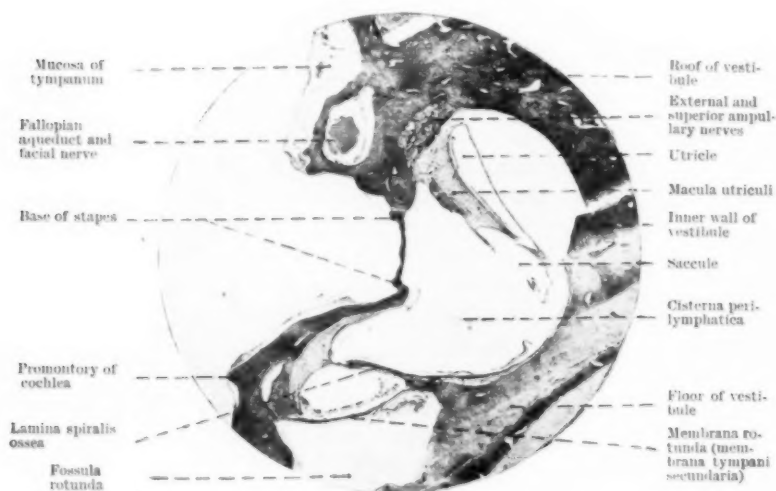


FIG. 1.

Vertical transverse section of the normal petrous bone through both fenestrae of the labyrinth.*

* Originally described in the *Journ. of Anat. and Physiol.*, 1909, xliii, pp. 329-45, "The Anatomy of the Human Labyrinth."

tympanum. The labyrinthine fluid which is in contact with the base of the stapes and with the membrana secundaria of the fenestra rotunda is subjected to the same variations in tension as those produced in the ossicles and air in the tympanum by the vibrations (fig. 1). The "thrusters and pulls" of the waves of sound are conveyed to the labyrinthine fluid simultaneously through the mobile portions of the inner tympanic walls, namely, through the fenestra ovalis and fenestra

rotunda, producing in the labyrinthine fluid corresponding variations of stress. "Stress" here relates to Newton's first law of motion, namely, "When a particle or one portion of matter acts on another portion so as to influence its state then the whole phenomena of the mutual actions of the two particles is called a stress."

The essential mechanism of the sound stimulus consists, then, of the reaction set up in Corti's cells by the impressed force acting through the medium of the membrana tectoria upon the hair-fibrils (fig. 2). Such

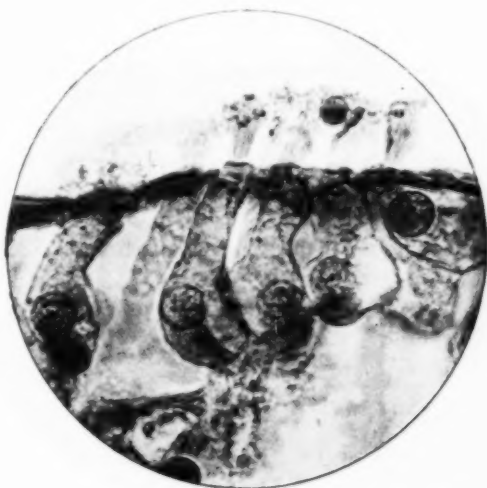


FIG. 2.

Fig. 2.—Radial section of the organ of Corti, showing fibrillae of hair-cells. (Photomicrograph magnification 1,000.)*



FIG. 2A.

Fig. 2A.—Schematic representation of a middle hair-cell, displayed to show the arrangement of the fibrillae.† The membrana tectoria (not shown) normally rests upon the ends of the fibrillae, which appear to be placed most favourably for the transmission of variations of pressure in the labyrinthine fluid through the medium of the membrana tectoria to the intracellular protoplasm of Corti's cells.

* Previously published in *Proceedings*, 1909, ii (Otol. Sect.), p. 31.

† From the *Journ. of Anat. and Physiol.* (vide supra).

variations in stress would be communicated to the perilymph of the scala tympani and of the scala vestibuli simultaneously, and act through the endolymph and medium of the membrana tectoria and supporting

structures of the cells of Corti, upon the free ends of the cilia of the hair-cells, synchronously throughout the whole of the organ of Corti. It is claimed that the physical stress must equally affect the whole of the organ of Corti, and that it is quite possible that higher centres are physiologically more sensitive to some particular "stress-complex" than to some others. These stresses would vary in intensity, frequency and complexity in accordance with differences in frequency, regularity, phase, amplitude, of simple and compound waves of sound. It is to the action of such stresses upon the protoplasm of the cells of Corti that we attribute the stimuli which evoke auditory sensations. The different sensations produced by sounds emitted by forks of different vibration-frequency are distinguished in the sensorium as differences of tone or pitch. The character of sound is determined, as is well known, by the precise combination or compounding of tones of different pitch, amplitude and phase, terms which are used in accordance with their accepted physical significance. One of the great difficulties which stands in the way of such an hypothesis is the occurrence of "gaps" in the auditory field of tone-range. The lowest frequency fork capable of producing a tone-sensation corresponds to sixteen double variations (or only slightly less). What the highest vibration-frequency producing tone-appreciation is has been difficult to determine. It will suffice for the moment to admit a high limit to the range of tone-appreciation. Between the highest and lowest limits of perception we include all tones in the term "tone-field," or "auditory field." A certain minimal intensity is requisite for a vibrating fork to produce a tone-sensation. The estimation of the "minimal intensity" is one mode of ascertaining "tone-acuity" in mathematical terms (*see* Charts).

The quality "loudness" may be regarded as an expression of the energy of the sound-wave, and physicists speak of loudness as varying directly with the energy of the sound-wave. But the consciousness of variations in loudness does not depend wholly upon the mathematical differences in intensity or energy of sound-waves. A consideration of Weber's and Fechner's physiological laws and of Wundt's hypothesis bears testimony that the question is not a purely physical one, but is one which involves psychical and mental processes; in fact, we find ourselves confronted by complex problems involving a consideration not only of physical energy and physiological stimuli, but of the sensations of consciousness and of differences of consciousness, of judgment and other psychical phenomena, which show that we are merely on the threshold of far-reaching investigations.

The energy which a given fork is capable of dispersing depends on its mass and on the amplitude with which it is made to vibrate. Of two forks of equal mass but different pitch, greater energy is necessary to produce vibrations (of the same amplitude) in the higher than in the lower fork. The dispersion of the energy of each fork to the surrounding medium is not necessarily directly proportionate to that put into the forks, for we must take into consideration the time occupied in the output, that is, the rate of decrement of amplitude of the vibrating instrument, and also the internal friction which would depend upon the mass and material of the fork as well as on its frequency of vibration.

It is not convenient in the application of such hearing tests as those we contemplate to utilize the sound produced by plucking a harp string,

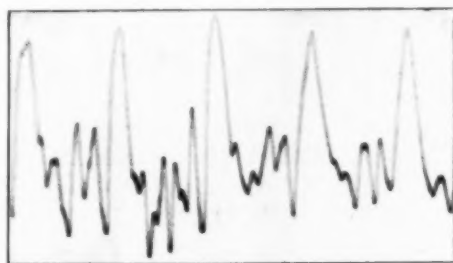


FIG. 3.

bowing a 'cello, or ringing a bell. The sounds produced by these instruments are composite, and we are unable to tell which of the numerous tones and over-tones generated are the ones which evoke sensations when the hearing is defective. Reeds and whistles produce complex tones. The human voice is also composed of compound tones, with different fundamentals, and many combined tones, having variable amplitudes. The accompanying photograph (fig. 3) represents an oscillogram of the disk of a telephone-receiver produced by the sound "Ah . . ." spoken into the transmitter. This record was taken with an oscillographic apparatus made by Messrs. Paul, devised by Mr. Irwin at the Imperial College of Science of Technology. The curve resembles that produced on the phonograph and analysed by Bevier according to Fourier's theorem. Bevier showed that the order of the harmonic which possesses the maximum amplitude varies with the pitch of the

fundamental note on which the vowel "ah" is sounded or sung into the phonographic recorder, but the *pitch* of the harmonic which has the greatest amplitude always lies between 1,000 and 1,300 double vibrations per second, the maximum effect occurring when one of the harmonics has a frequency of about 1,150 vibrations. In the same way Bevier found that the sound "I . . .," as in "It," contains a single harmonic of frequency about 1,850, which is very strong in amplitude, harmonics of about 575 fairly strong, and harmonics between these frequencies which are very weak. Again, the amplitude of the fundamental varies considerably according to pitch. If the frequency is 200 or over 500, the amplitude is great; if the frequency lies between 275 and about 450 the amplitude is small.¹

The foregoing considerations seem sufficient to indicate the importance of selecting sound generators for hearing tests which produce only pure simple tones. Tuning forks with inertia clamps, and particularly those made by Edelmann, give the purest tones with which to examine the low limit of the "tone-field." Single tones of high frequency can be produced by straight glass tubes in which longitudinal vibrations are set up by means of friction. The glass tube of suitable length is held in the fingers near the middle, while the tube is rubbed with wash-leather moistened with methylated spirit or turpentine. Mr. Frederick Womack has kindly set up for me for experimental purposes a series of brass tubes clamped in the middle to a frame, and these can be used more conveniently than glass. The pitch of the sound produced depends upon the length of the tube, as well as on the material of which the tube is composed. A brass tube of 168 cm. long emits a tone of approximately 1,024 d.v. per second. The production of harmonics is avoided by carefully stroking the tube, but only with difficulty in a tube so long as this. The tube of half this length, namely 84 cm., emits a tone corresponding to c^4 (2,048 d.v.), and so on.²

The highest audible tones which can be produced by means of these tubes are about 18,000 d.v. per second. Schultze employed a steel wire fixed at each end in place of rigid rods supported in the middle. Van

¹ Compare modern text-books on physics, which quote Bevier's investigations—e.g., W. Watson, "A Text-book on Physics," 1911, London.

² As Mr. Womack found, the tubes are made to "speak" more easily if one employs a wash-leather glove, the forefinger and thumb of which are moistened with turpentine mixed with a little powdered resin, which is gently drawn along the outer third of one end of the tube.

Struycken devised a simple form of instrument with a wire of 50 cm. long, supported in a steel frame resembling that for a fret-saw. This is preferable to Schultze's, but depends on the same principle. Messrs. J. J. Griffin have made for experimental use a similar instrument which

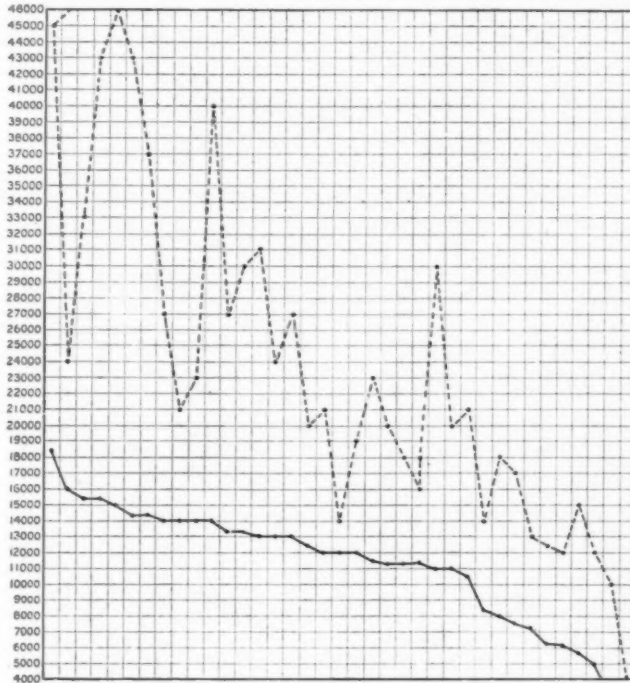


FIG. 4.

Comparison of the results of testing for the high tone limit by means of Edelmann-Galton whistle, and Van Struycken's steel monochord. Each column presents the results of both tests applied to one ear. It will be seen that the Edelmann whistle always gives the higher reading, but the results do not tally proportionately. A comparison of the physical properties of whistles with those of short, tense steel wires vibrating longitudinally, leads one to place more reliance on the latter instruments and to accept the lower reading as the more accurate.

has the advantage that it can be folded up into a small compass, and when open is 1 m. in length, so that we can obtain tones from 2,500 to 18,000 d.v. by adjusting the movable clamp.

During the past year a series of observations have been made with these instruments, the results of which are shown in the accompanying charts. When we compare the highest tones on the Edelmann-Galton whistle with those produced by the steel monochord we find different results (*see* fig. 4). The comparison of physical and clinical observations leads us to infer that the highest perceptible tone for practical purposes corresponds to sound-waves possessing a frequency of 16,000 to 20,000 d.v. per second. Although the Edelmann-Galton whistle apparently produces these tones, the sounds are so mixed with other high tones, some of which probably possess a greater amplitude than that having the highest pitch, which is thus blotted out from consciousness.

Rinne's Tuning Fork Test.—In the test as usually applied the duration of hearing the sound transmitted to the air by the limb of the fork is compared with the sound transmitted to the bone by the stem of the fork. Now the energy of the sound produced by the limb of the fork is always greater than that which is synchronously produced by the stem. It is hardly necessary to say that the sound transmitted by the stem is not "conducted through the fork from the limbs" but depends upon the position of the nodal points at the base of each limb. The farther apart the nodal points the greater is the amplitude which it is possible to produce in the vibrations of the stem of the fork. Conversely, the nearer the nodes are together the less the amplitude of vibration which is possible in the stem. In low-pitch forks the nodal points are farther apart than in high-pitch forks; hence the well-known dictum that "bone-conduction appears to diminish as we ascend the scale" is explained by physical properties of the instrument employed. In the high forks there is no sound generated at the stem, and that is the true reason why sound-sensations fail to reach the ear. If instead of using a fork for testing bone-conduction we employ the monochord, we find that true bone-conduction is practically equal or better than air-conduction, even for tones of over 16,000 d.v. per second (*see* Tables).

Schwabach's test may be regarded as a "tone-acuity" test through the medium of bone-conduction. The difficulties in applying it are due to the impossibility of satisfactorily avoiding bilateral stimulation, even by the use of noise generators to exclude one ear, while applying the fork to the mastoid surface of the other.

Weber's Test.—When we apply the fork to the middle of the vertex by Weber's method more sound-energy may reach one ear than the

other, in which case the sensation of loudness is lateralized to the side which transmits the stronger stimulus.

Dr. Barr has considered the clinical aspects of the bone-conduction tests, and I shall therefore merely add some remarks concerning the mechanism of so-called bone-conduction which has a particular bearing on the hypothesis which has been submitted for deliberation earlier in this paper.

The Mechanism of "Bone-conduction." — When the base of a vibrating tuning fork of suitable pitch and amplitude (say c^1), or else the steel monochord, is applied to the head, the sound-waves are transmitted to the cranial bones, which vibrate in harmony. We must not overlook the well-known fact that the thickness of the scalp varies in different persons and will affect the observations in comparing extreme conditions; it is also open to remark that constant pressure with the instrument against the skull is not maintained in the ordinary method of applying bone-conduction tests. Nevertheless, in practised hands the variations due to these difficulties are probably not very great. The skull as a whole becomes a sound transmitter, imparting its vibrations to the surrounding media—namely, to the air in the air-containing cavities, to the fibrous tissues, ligaments and muscles, &c., in contact with the cranium. Thus the fork or monochord through the bone produces vibrations of the air in the meatus and tympanic cavities, which are conveyed to each labyrinth by the fenestra rotunda and fenestra ovalis as in the case of ordinary air-conduction. Now in certain morbid conditions the air in the tympanum is displaced by some other medium—e.g., mucus, serous effusion, pus, swollen muco-periosteum or granulation tissue—and vibrations of sound are conducted through these media with a loss of energy which varies inversely with the density of the medium. Hence in these conditions a greater proportion of the energy which is dispersed by the fork when applied to the skull acts on the labyrinthine fluid and the sense of hearing is lateralized to the side which receives the stronger stimulus. This is upheld by the familiar results of Weber's test in unilateral deafness in circumstances free from special difficulty. Certain conditions of unilateral middle-ear disease are associated with the lateralization of the fork to the normal side. Is it permissible to presume "nerve degeneration" on the affected side resulting from disuse? I cannot help thinking our data are insufficient to support such an inference, especially when the activity of the vestibular functions of the labyrinth persists.

Apart from psychical considerations which may be invoked to explain

the difficulties patients often experience in attempting to describe their sensations, it is quite possible that physical considerations will serve to explain such lateralization by Weber's test to the normal side in pure middle-ear affections of the other side. For instance, we should be prepared to find that in cases of bone ankylosis of the stapes and *complete* obliteration of the oval window, that bone-conduction from the vertex produces the stronger stimulus in the normal ear. I am, so far, unable to make any statement of fact on this point, but possibly others may have something to say about it during the discussion.

Among the fascinating phenomena observed in studying the significance of the hearing tests is the occurrence of tone-gaps and tone-islands in the range of the auditory field. We meet with numerous instances of this peculiarity when we study the acuity of hearing in very deaf subjects with Bezold's continuous tone generating instruments. In the tables a few examples appear, but I cannot yet feel satisfied that the instruments with which the tests were made are all free from error, and I regard the occurrence of "gaps" and their correct limitations to be in need of re-investigation by means of additional monochords and resonators, before we should accept the observations as reliable data. I have under observation at present what appear to be undoubted examples of gaps and islands, but I do not feel prepared at the present time to uphold any satisfactory exposition. I hope that the presentation of a series of records of actual cases may prove of some service.

I thank you, Sir, and the Council for inviting me to share the honours of opening the discussion with Dr. Thomas Barr, and I thank members present for the kind way they have attended to the observations which I have made. I share the feeling which has often been expressed that the subject is an exceedingly difficult one, and any suggestions and hypotheses here presented are laid down merely for discussion and consideration, without any pretentious claim that they represent the last word on a matter which can only be adequately dealt with by the von Helmholtz of the future.

APPENDIX.

The records which follow are appended for the sake of illustration and reference. They include many common conditions as well as those which are more rarely met with. Several examples are added of patients who have been tested during life and have subsequently died, and whose temporal bones have been examined pathologically.

Among other examples was that of a man who was "stone deaf" and in whose right temporal bone was found the remnants of past otitis media, with obliteration of both labyrinth windows by cicatricial tissue. Serial sections of the inner tympanic wall were cut, and wax plate models of the sections have been prepared, and are presented to show more clearly the exact state of affairs.¹

Another patient was tested on several occasions during the latter days of her life, the last occasion being the day before she died.¹

A third instance in which an examination was made before death was that of a deaf-mute whose brain has been described by Dr. Fortuyn in the *Archives of Neurology*, 1911. I tested the hearing four months before death, and have since examined the labyrinths and middle ears pathologically.¹

Four other examples of deaf-mutes are also referred to, but the full results have not yet been prepared.

¹ The details of these cases will be given at a subsequent meeting.

EXPLANATION OF CHARTS.

CHART I: GROUPS 1 TO 6—VARIOUS TYPES.

- (1) Normal duration of hearing by air-conduction each of the eight forks used in the tests. The numbers in the left-hand column represent seconds; the numbers and lettering at the top of the charts indicate the pitch of the fork in the numerical, English and German system of notation.
- (2) W. F., aged 19. Acute mastoiditis which developed four weeks after the onset of acute otitis media. Hearing tested about four months after Schwartz operation. There was then a white opacity in the upper posterior quadrant of the left tympanic membrane corresponding to the site of a healed perforation. In response to conversation tests and to the watch hearing appeared to be normal on both sides, but testing with low forks revealed some loss of acuity on the left side.
- (3) K. M., aged 40 (1908, St. Bartholomew's Hospital). Deafness progressively worse for last four years; onset began with "cold in the head"; tympanic membranes intact. Watch: right 2 in., left on contact only. Rinne: 256 d.v., right positive, left negative. Weber to right. The chart represents acuity tests for the left ear by air-conduction.
- (4) F. W., aged 16 (1908, St. Bartholomew's Hospital). Deafness and "atrophic rhinitis"; tinnitus like "bells ringing"; tympanic membranes intact. Watch: right 12 to 18 in., left 14 in. (? "catarrhal deafness").
- (5) J. C., aged 66 (1908, St. Bartholomew's Hospital). For five years increasing "hardness of hearing"; tympanic membranes normal; Eustachian tubes clear. Watch: right 1 in., left 4 in. (instead of 4 ft.). Bone-conduction, with base of fork on mastoid, meatus gently closed (Bing's method), showed loss as follows: 64 fork inaudible (or indistinguishable from the humming noise produced by meatal compression); 128 fork, -15 seconds; 256 fork, -25 seconds; 512 fork, -35 seconds; 1024 fork, -15 seconds; 2048 fork, inaudible. Early type of Galton whistle, tone-limit 2.
- (6) E. H., aged 34 (1908, St. Bartholomew's Hospital). Chronic suppurative otitis media, right side, for ten years; tinnitus and deafness in left ear for one year; left tympanic membrane intact; right membrane, large perforation and granulations in inner tympanic wall. Chart indicates acuity of hearing after inflation per catheter. Watch: right 2 in. out of 48 in., left 4 in. out of 48 in. Weber (256 fork) to right side. Rinne: right positive, left negative. Gellé: right positive. Caloric tests positive. Diagnosis ?

CHARTS II AND III: GROUPS 7 TO 12 AND 13 TO 18—SYPHILITIC TYPES.

- (7) M. Z., aged 29 (1908, St. Bartholomew's Hospital). Complains of deafness, tinnitus and dizziness for many years; a few years ago attacks of vertigo; tinnitus worse lately. She has a healthy child, aged 3. The patient has peculiar teeth and very slight signs of interstitial keratitis; the tympanic membranes are intact. The chart indicates acuity tests for right ear, air-conduction.
- (8) Left ear, same patient, air-conduction.
- (9) Right ear, same patient, bone-conduction.
- (10) Left ear, same patient, bone-conduction. Rotation tests indicate greatly diminished or negative response on the right side.
- (11) A. S., aged 29 (1908, St. Bartholomew's Hospital). Deafness and tinnitus at least five months; tympanic membranes atrophic in appearance. Watch: right 3 in., left 6 in. Rinne: positive right and left. Schwabach: negative right and left. Weber, nil. Gellé, negative response. Chart shows reaction for the right ear.
- (12) Left side gave similar results, but with greater loss for low tones and less for high; this tallies with the greater acuity for the watch in the left ear.

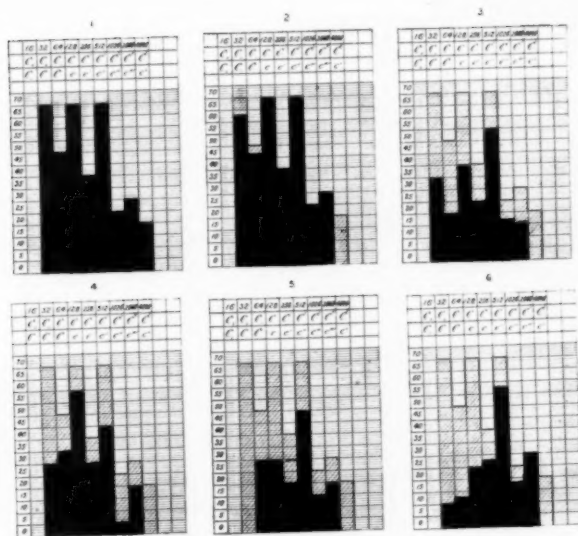


CHART I.

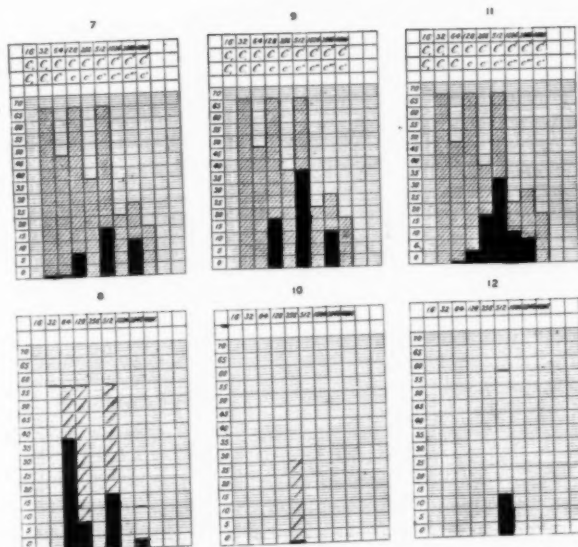


CHART II.

120 Scott: *The Value and Significance of Hearing Tests*

CHART III.

- (13, 14, 15, 16) T. K., aged 21 (1909, St. Bartholomew's Hospital). Deafness and tinnitus, right ear, five years; left ear, nine months; tympanic membranes intact. Watch inaudible. Tinnitus "clashing, squeaking, humming, buzzing, rumbling, hissing, whistling." Diagnosis, ? syphilis.
- (13) Right, air-conduction.
- (14) Left, air-conduction.
- (15) Right, bone-conduction.
- (16) Left, bone-conduction.
- (17 and 18) W. L., aged 21 (1908, St. Bartholomew's Hospital). Nearly "stone deaf"; tympanic membranes opaque and retracted. Watch: right *nil*, left 3 in. Caloric tests, rotation tests, negative. Galvanic tests, active nystagmus produced by anode and kathode on the left side. Three months later absolutely deaf for all forks, air- and bone conduction. (Not tested with Edelmann instruments.) Has interstitial keratitis, and peculiar upper incisors.

CHART IV: GROUPS 19 TO 24—SUPPURATIVE OTITIS MEDIA.

- (19) L. R., aged 14 (1908, St. Bartholomew's Hospital). Deafness and otorrhœa, right ear, following scarlet fever eighteen months previously; small attic perforation right membrane. Acoumeter heard 8 in. No loss of bone-conduction for forks below 256 d.v.
- (20 and 21) E. F., aged 14 (1908, St. Bartholomew's Hospital). Has had bilateral otorrhœa since infancy; polypus removed from right ear when aged 8; tonsils removed when aged 8½; right membrane replaced by granulating mass; left membrane destroyed and scarred. Watch: right 15 in., left 24 in. Gellé, positive reaction. Schwabach, -15-30 seconds for forks 128 : 256 : 512 d.v.
- (22 and 23) J. S., aged 30, a bassoonist (1908, St. Bartholomew's Hospital). Progressive deafness for last twelve months; had bilateral otorrhœa ten years ago; tympanic membranes show opacities at site of old perforations; nose and Eustachian tubes normal. Watch: right 5 in., left *nil*. Weber to right. Acoumeter: right 3 in., left 1 in. Gellé negative. No loss of bone-conduction.
- (24) G. J. (1908, St. Bartholomew's Hospital). Scarlet fever at the age of 4; diphtheria at the age of 12; chronic otorrhœa right side at least three years; tympanic membrane perforated and sessile granulations visible on floor of tympanum. Gellé positive. Caloric tests normal. Chart shows reactions for right ear, air-conduction.

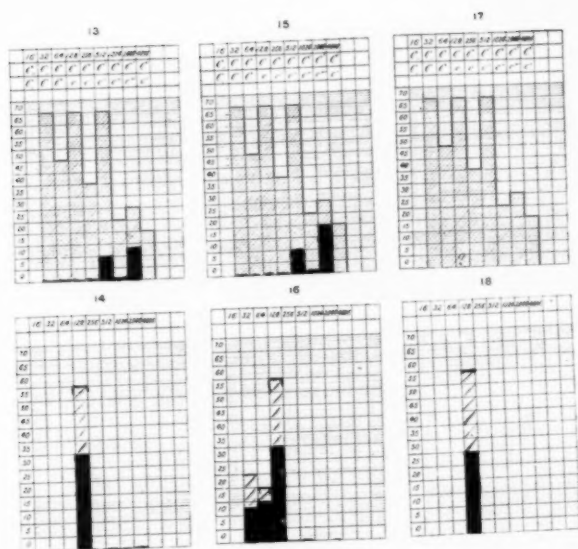


CHART III.

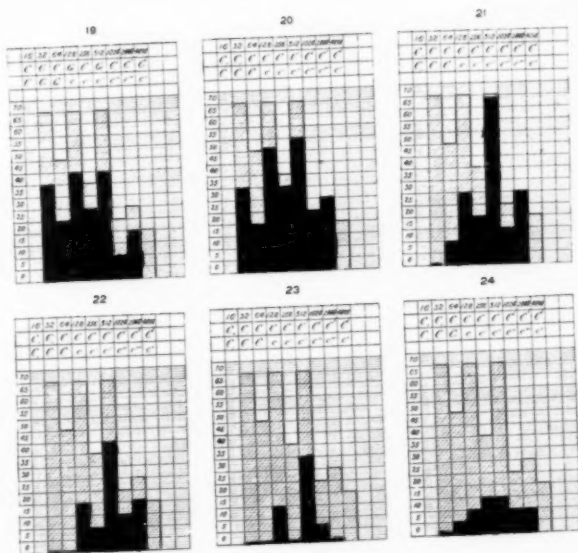


CHART IV.

CHART V: GROUPS 25 TO 30—TYPE WITH UNILATERAL ABSOLUTE DEAFNESS.

- (25 and 26) G. A., aged 34, a pianoforte tuner (1909, St. Bartholomew's Hospital). Has had bilateral otorrhea since childhood. May, 1908, sudden giddiness; laid up with severe giddiness several weeks; detained in infirmary; was told it was due to "nervous debility." August, 1908: able to get about; attended an ear clinic; gradually lost sense of giddiness, except on very sudden movements of head; had become absolutely deaf in left ear; both tympanic membranes gone, replaced on left side by fibrous polyp, and on right by granulations springing from inner tympanic wall. Weber to right side. Hearing tests: right ear, those of ordinary middle-ear deafness not very severe. Chart shows hearing reactions for air (25) and bone (26) in the left ear. It is suggested that the responses are due to the perception by the right side. Caloric tests: left ear negative in all positions of head; right side positive all positions. Rotation reactions for left ear, all positions negative. Rotation tests normal for each canal on right side. Application of probe to region of right stapes induced dizziness; no nystagmus or dizziness produced by compression of meatus.
- (27 and 28) E. S., aged 18 (1907 and 1908, St. Bartholomew's Hospital). Scarlet fever at the age of 7; no very noticeable deafness, but Weber to left ear. Rinne neutral left side; right side normal. Complaints of "thumping" tinnitus in left ear; giddiness and headache. Patient has already had two operations for adenoids elsewhere, and some are still visible high in vault (Chart 27). Left ear, air-conduction (28), bone-conduction eight months after left ossiculectomy. Weber's test is now to right side instead of to left. The thumping tinnitus is replaced by loud rushing noise, which increases for periods of two or three minutes at a time. Rotation tests, and caloric reactions negative left side.
- (29 and 30) T. H., aged 20 (1908, St. Bartholomew's Hospital). Bilateral chronic otitis media. Twelve months ago he had a mastoid operation on left side, which, he says, was followed by facial palsy and deafness, which persist; it is impossible to ascertain whether the palsy was not of longer duration. Charts 29 and 30 represent air- and bone-conduction, left ear. Weber's test is to the right. Rinne negative, right and left. Watch: right 2 in., left *nil*. Schwabach: negative right and left for c , c^2 and c^3 . (No notes of vestibular reactions.)

CHART VI: GROUPS 31 TO 36—TYPES SHOWING RESULTS OF OPERATIVE PROCEDURES.

- (31) T. L., aged 22 (1908, St. Bartholomew's Hospital). Chronic suppurative otitis media, right side, since childhood; had to leave Navy on that account. Watch: right side 1 in., left 4 ft. Weber to right side. Gellé's test, 256 fork: meatal compression, right side, diminishes bone-conduction. After radical operation, hearing tests shown in Chart 34 (see below).
- (32 and 33) S. A., aged 28 (1909). Chronic suppurative otitis media right side for fourteen years; left side normal; right tympanic membrane gone; granulations and fibrous tissue in tympanum. Watch: right *nil*, left over 4 ft. (hyper-acute). Rotation and caloric tests, normal both sides. Weber to left side. No Gellé or "fistel" symptom. Apparent loss of appreciation for forks in right ear, by air- and bone-conduction, suggesting labyrinthine deafness, but vestibular reactions normal. Charts show hearing tests for air- and bone-conduction, right side, before operation. (See Charts 35 and 36 for reactions after operation.)
- (34) (See Chart 31.) Hearing reactions, after operation.
- (35 and 36) (See Charts 32 and 33.) Hearing tests in right ear, after radical operation; no fistula of vestibule or cochlea; stapes intact; dense mass of fibrous tissue occupying the sinus of the tympanum and occluding the fossula rotunda. This tissue removed with unexpected results, attributed to the previous occlusion of the round window. (Compare Charts 32 and 33, before operation, with Charts 35 and 36, after operation.)

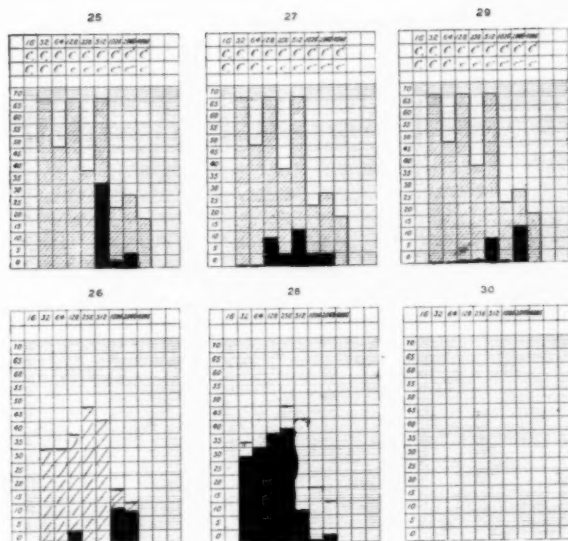


CHART V.

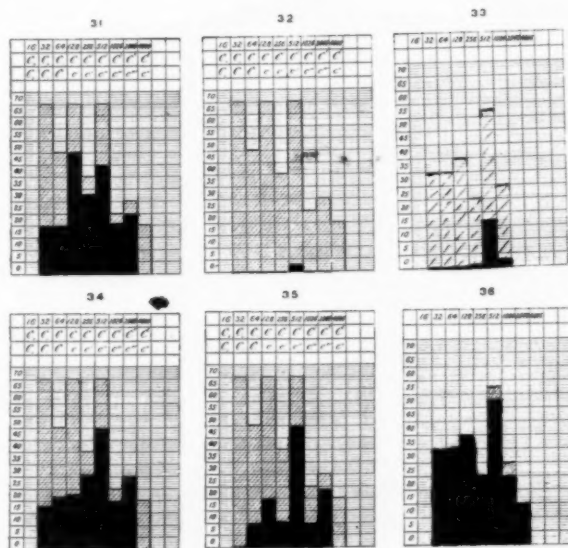


CHART VI.

TONE RANGE TEST.

BRIEF NOTES OF CASES IN CHARTS VII, VIII, AND IX.

- (1) W. D., aged 37, a tabetic. Tympanic membranes intact; Eustachian tubes clear. Rinne: right +10 seconds; left -7 seconds. Schwabach: right -12 seconds; left +15 seconds. Weber from vertex and from left mastoid lateralized to right side. Acoumeter: right 10 cm., left over 7 m.
- (2) J. D., aged 22. Quite well until between two and three years ago, then tinnitus, giddiness, and deafness; tinnitus persists, varies in intensity, often very loud; can hear raised voices close to left ear, and raised *tête-à-tête* in right ear; in each case hearing

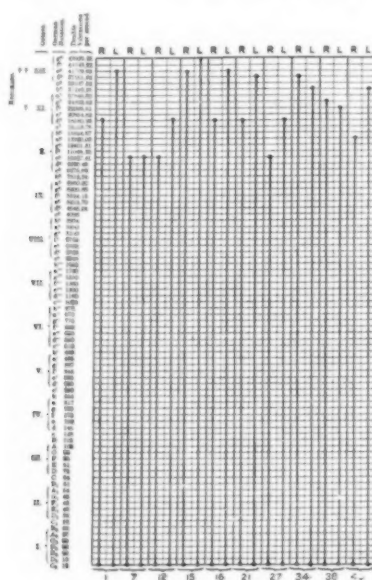


CHART VII.

Table showing the tone-range in ten patients, estimated by means of Bezold-Edelmann forks and Galton-Edelmann whistles. This group has no loss of low tone perception in either ear. (Tests applied at the National Hospital, Queen Square.)

with the opposite ear excluded with Bárány's noise apparatus; tympanic membranes and Eustachian tubes normal. Schwabach (Bezold-Edelmann *e'*): right -50 seconds, left inaudible; *e''* and *e'''*, right inaudible, left inaudible. Wassermann negative. Central nervous system normal (Dr. Buzzard).

- (3) H. E., aged 27. Deafness and tinnitus in left ear for nine months. Ménière attacks, diagnosed at first as influenzal. Wassermann positive. Rinne: *e*, right +25 seconds; left -10 seconds. Schwabach: *e* (per auscultatory tube), right neutral; left -12 seconds. Weber to right. Hears worse in a noise. Was injected partly intravenously and partly subcutaneously (not intramuscularly) with "606." Slight attacks of vertigo occurred six weeks later, and Wassermann still positive. Patient unwilling to have injection repeated although advised to have a second trial. Hearing *in statu quo*.

- 4) W. E., aged 69. Ménière attacks. Rinne: 90 d.v., right and left positive; 217 d.v., right negative, left positive. Schwabach: e^2 , right inaudible, left inaudible. Conversational voice 2 m., approximately 1.5 m.
- * (5) W. F., aged 37. Examined four weeks before death. Tympanic membranes and Eustachian tubes normal. Caloric tests: right negative, left normal reactions. Schwabach: e^1 , right -5 seconds, left normal; e^2 , right -25 seconds, left normal. Rinne: right negative, left positive. Weber, doubtfully lateralized to left. Autopsy: "auditory nerve tumour" right side; sections of nerves and of decalcified labyrinths show the tumour does not invade the labyrinth.

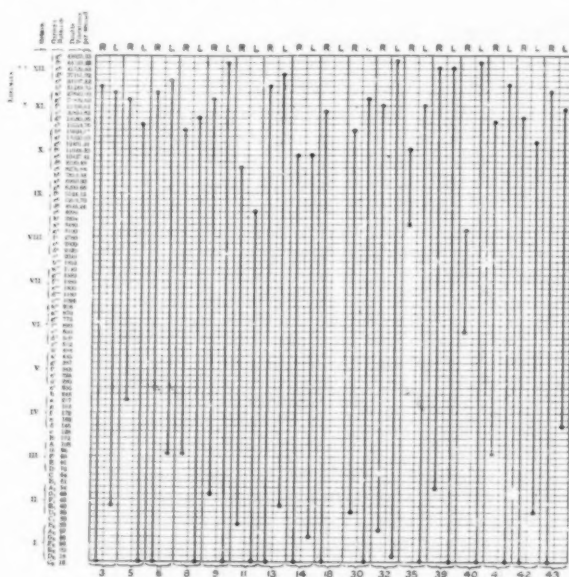


CHART VIII.

Table showing the tone-range in seventeen patients, estimated by means of Bezold-Edelmann tests and Galton-Edelmann whistles. In this group the low tone limit is raised in one ear, while the other side retains perception for low tones.

- (6) R. F. Left tympanic membrane scarred and adherent to inner wall. Rinne: e , right +, left -. Schwabach: e , right -6 seconds, left -3 seconds. Weber to left side.
- (7) W. F. Rinne positive: Schwabach negative both sides. Rotation tests and Bárány's post-rotatory "pointing tests" normal.
- 8) H. F., adult. Chronic suppurative otitis media right side. Left tympanic membrane and Eustachian tube normal; complains of constant "rushing" and "pulsating" tinnitus day and night, chiefly left ear. Rinne: e^1 , right -35 seconds, left neutral. Schwabach: right normal, left +5 seconds. Voice: Loud at 3 ft. Bezold-Edelmann, fork e^2 : inaudible right side at maximum amplitude, close to ear; whistle, e^2 , audible right and left side. (Right vocal cord fixed.)

* Cases marked thus * (5) were also investigated post-mortem.

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- (9) L. G., aged 26. Six months previously was being treated for sore throat when she got herpes of pinna, right side; then, a week later, sudden complete right facial palsy and deafness, and for ten days giddiness and vomiting. Caloric, galvanic, and rotation tests: right negative, left normal. Hearing—Rinne: e, right negative, left positive. Schwabach: e, -15 seconds, left -5 seconds (ordinary method); right -10 seconds, left normal (per auscultatory tube). Weber indeterminate. Acoumeter: Less than 10 cm. right, more than 7 m. left.
- (10) E. G., aged 38, a parlourmaid. Deaf seventeen years with tinnitus, "pulsating" and "singing," which began with diphtheria; tympanic membranes and Eustachian tubes normal. Rinne: e', right and left negative.
- (11) S. G., an elderly woman. Headaches, tinnitus, deafness, and giddiness for two years; no disease of central nervous system (Dr. Grainger Stewart); right tympanic membrane cupped. Eustachian catheter produces no change. Schwabach's test: e', right positive, left neutral. Weber: a, referred to right; e', referred to left.
- (12) E. H., aged 24. Under the care of Dr. Ormerod with symptoms of "bulbar palsy." Hearing: tympanic membranes and Eustachian tubes normal. Rinne: e', right +10 seconds, left +12 seconds. Schwabach: right -10 seconds, left -14 seconds. Weber: e', referred to right side. Tone-intensity tests: Bezold-Edelmann forks (air-conduction), 90 d.v., right -20 seconds, left -10 seconds, normal duration 70 seconds; 145 d.v., right -57 seconds, left -45 seconds, normal duration 145 seconds; 217 d.v., right -22 seconds, left -12 seconds, normal duration 40 seconds; 290 d.v., right -30 seconds, left -18 seconds, normal duration 90 seconds; 435 d.v., right -35 seconds, left -20 seconds, normal duration 80 seconds; 580 d.v., right -45 seconds, left -30, normal duration 55 seconds. Rotation tests normal.
- (13) J. A. H., aged 42. Under the care of Dr. Taylor, with symptoms of paralysis of the right tenth, eleventh, and twelfth cranial nerves, the right half of the tongue, of soft palate, and the right vocal cord being paralysed; both tympanic membranes perforated; left side covered with thin scar, right perforation unhealed; mucosa of inner tympanic wall visible. Rinne: e, -20 right and left sides. Weber to left side. Schwabach not negative. Rotation tests normal. Whisper: right 2 m., left 10 cm.
- (14) W. F. H., aged 51. General nervous symptoms resembled those of tabes; tympanic membranes and Eustachian tubes normal. Rinne: e, right +23 seconds, left +25 seconds. Schwabach: right -22 seconds, left -20 seconds. Air-conduction; e', (Bezold-Edelmann), right -45 out of 55 seconds, left -40 out of 55 seconds. Weber indefinite. Rotation tests: normal post-rotatory nystagmus; rapid turnings ten times in 20 seconds produced no deviation in pointing tests.
- (15) H., a man under the care of Dr. Tooth. Tympanic membranes and Eustachian tubes intact. Rinne positive and Schwabach negative both sides. Watch audible 1 m. right side and 0.75 m. left side (normal 1.25 m.). Rotation tests: normal nystagmus reactions; normal deviation reactions after clockwise rotation, head erect; no deviation reaction after counter-clockwise rotation; tested twice.
- (16) E. I., under the care of Dr. Batten, with symptoms of neurasthenia. Tympanic membranes normal. Rinne: a, right +20 seconds, left +20 seconds; second test, right +30 seconds, left +25 seconds. Schwabach: a (first test), right -15 seconds, left neutral; (second test), right -12 seconds, left -12 seconds; (third test) right -20 seconds, left -18 seconds. Air-conduction: first test, right -10 seconds, left -3 seconds; second test, right -7 seconds, left -5 seconds; third test, right -20 seconds, left -15 seconds. Weber to left.
- (17) A. J., aged 41, a syphilitic with "pack-thread" pharynx, destruction of soft palate and absolute occlusion by scar tissue of the pharyngeal ends of the Eustachian tubes; Tympanic membranes intact, very cupped. Rinne: a, right -12 seconds, left -6 seconds. Schwabach: a, right -6 seconds, left -5 seconds. Weber indeterminate. Voice: audible when shouted at 3 ft., patient holding hand to ear. Rotation tests: normal reactions.
- (18) I. H. K., aged 41. Under care of Dr. Tooth, suffering from effects of head injury sustained in fall off tramcar; was unconscious four days; detained in infirmary three months; tympanic membranes intact, not cupped; no facial palsy. Rinne: right

side positive for a, e', and a'. Schwabach: normal right side. Weber: referred to right side with e, a, e', a', e'; forks on left mastoid referred to right. No tones in continuous tone series referred to left ear, either by air- or bone-conduction. Complains of loud "hissing" tinnitus in left ear. Post-rotatory and galvanic vestibular reactions obtained on both sides. Eustachian tube: right side normal, left side inflated with difficulty, as if partially occluded.

- (19) A. K., admitted to the National Hospital with "hysterical paraplegia," on recovery from which deafness developed; is not very deaf for conversational voice; can converse *tête-à-tête* with unraised voice. Rinne, negative right and left. Schwabach, negative right and left.

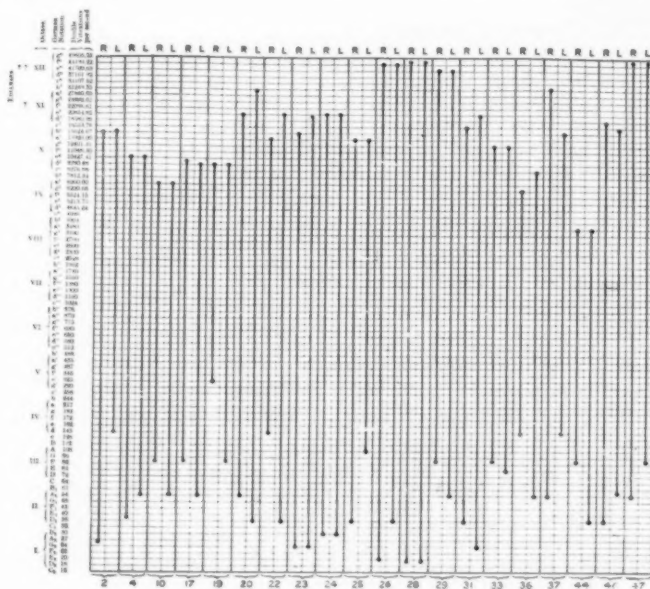


CHART IX.

Table showing the tone-range in twenty patients, estimated by means of Bezdold-Edelmann forks and Galton-Edelmann whistles. In this group the low limit of tone-perception is raised on both sides.

- (20) L. A., aged 34, under the care of Dr. Aldren Turner with neurasthenia and deafness; deafness attributed to frequent head colds ten years previously. Conversational voice audible at 1 ft. Tympanic membranes intact. Eustachian tubes clear. Rinne negative. Schwabach positive both sides. Complains of some tinnitus.
- (21) A. A., under the care of Dr. Grainger Stewart with "traumatic neurasthenia" of twenty months' duration. Rinne: e, right +15 seconds, left +20 seconds. Schwabach: right -10 seconds, left -5 seconds. Noticed to be giddy during ocular convergence. Mr. Paton reported "Eyes normal; muscle balance perfect; vision $\frac{5}{6}$." Rotation tests: hypersensitive reactions.
- (22) E. B., aged 42. Chronic suppurative otitis media and radical mastoid operation, right side, four years before present hearing tests. Weber, e to left side. Rinne, left side -10 seconds. Schwabach, normal left side. No tones audible by bone-conduction in right ear. (No note of vestibular tests.)

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- (23) E. B., aged 62. Ménière symptom-complex. Rinne, positive with e', a'. Schwabach, normal with e', a'. When testing bone-conduction by Rinne's method the patient refers the sound to the opposite ear, in each case to the end of audible bone-conduction (Bezold-Edelmann forks e', a').
- (24) W. B., aged 38. Deafness began one week after "influenza" four years previously; no earache. Rinne: e, negative. Schwabach positive. Weber not lateralized. Conversational voice about 3 ft. Acoumeter, 4 in. Gellé, negative reaction. Paracusis of Willis present.
- (25) D. B., aged 44, under care of Dr. Farquhar Buzzard for "psychasthenia"; feelings of depression, confusion, noises in head, and deafness, with nausea and vomiting; can hear *tête-à-tête* conversation, not general conversation. Rinne: a', right neutral, left negative; e', right and left negative. Schwabach: e', right and left positive. Acoumeter: right 0.5 m., left, 2 cm. Tympanic membranes intact. Eustachian tubes non-inflatable by politzerization or by catheter.
- (26) E. M. B., under the care of Dr. Aldren Turner for "neurasthenia." Complaints of deafness, especially left side; left tympanic membrane cupped; Eustachian tube clear. Rinne: e', right +10 seconds, left -10 seconds. Schwabach: e', right and left positive. Air-conduction: e', right -20 out of 90 seconds, left -40 out of 90 seconds.
- (27) J. T., aged 42. Hears "raised" voices at 3 ft. Rinne positive. Schwabach negative both sides. Acoumeter: right 8 m., left 1 m. Air-conduction: e', right -35 out of 90 seconds, left -40 out of 90 seconds; right -15 out of 55 seconds, left -11 out of 55 seconds. Tympanic membranes and Eustachian tubes normal.
- (28) A. B. Deafness improved by politzerization.
- (29) A. E. B., aged 42. Attended National Hospital under care of Dr. Risien Russell, with symptoms of intracranial tumour; tympanic membranes intact; nose normal. This patient could not hear a' to d' or e' to a' with the Bezold-Edelmann forks, but could hear the tones produced by Edelmann's large whistle corresponding to these notes. The tests were repeatedly confirmed, the forks vibrating at maximum amplitudes and held with limb close to meatus. Rinne negative. Schwabach normal or slightly negative (not "positive"). Raised voice: right 1 ft., left 3 in. (Vestibular tests omitted.)
- (30) L. B., aged 49, a veteran athlete, under the care of Dr. Farquhar Buzzard since 1907 with tabes, loss of sight and of hearing; Ménière symptom-complex fourteen years before tabetic symptoms recognized. Tympanic membranes: left normal, right only posterior half visible, owing to shape of meatus. Small quantity of pus in right meatus. Patient says he has been subject to a little discharge from the right ear for nearly ten years, from time to time. Rinne: e, a', e', a', e', right positive, left negative. Schwabach: e', right and left -15 seconds; meatus closed, -30 seconds. Air-conduction: e', right -35 out of 90 seconds, left -40 out of 90 seconds. Weber: heard equally well each ear. No blanks in "tone-range." Voice, 2 m. away, imperfectly; "raised voice," about 0.5 m. Acoumeter: right 2 cm., left 4 cm. Galvanic vestibular nerve reactions normal.
- (31) W. B. Post-influenzal deafness five years ago; tympanic membranes and Eustachian tubes clear; nose natural, can hear *tête-à-tête*; hears better in a noise.
- (32) E. A. C., aged 34. First seen June, 1911. Ménière symptom-complex noticed two and a half years previously; treated with catheter without effect. Rinne: e, right +30 seconds, left -5 seconds. Air-conduction: right normal, left -35 seconds (145 seconds normal). Schwabach: e, right normal, left -10 seconds (per auscultatory tube). Weber to right side. Eustachian tubes not obstructed (catheter test).
- (33) G. C., aged 58, under the care of Dr. Grainger Stewart for tabes, which was first noticed four years previously; optic atrophy present (Mr. Paton); tympanic membranes and Eustachian tubes normal. Rinne: e, negative. Schwabach: +10 seconds. Rotation tests: normal reactions. Can hear *tête-à-tête* conversation.
- (34) G. C. Under the care of Dr. Gordon Holmes with symptoms of paralysis of the fifth, sixth and seventh cranial nerves, right side. Sensations in the right meatus for touch, pain, and heat, are dull. Hearing tests applied in January, 1910, showed the

- right cochlear nerve free. In August, 1910, the hearing was found to be affected. Rinne: e', right and left positive (January); right negative, left positive (August). Schwabach: e', right and left normal (January); right -20 seconds, left normal (August). Weber to left. Vestibular tests normal. Bárány's pointing tests normal.
- (35) C. C., under the care of Dr. Grainger Stewart with symptoms resembling those produced by extra-cerebellar tumour; deafness and tinnitus in right ear; can hear ordinary conversation in left ear. Galvanic reactions: negative right side, active left side. Weber to left. No tones heard by bone-conduction right side. Schwabach: g', left -65 seconds (per auscultatory tube).
- (36) I. C., under the care of Dr. Batten, with facial palsy; tympanic membranes and Eustachian tubes normal; deafness and pulsating tinnitus in left ear. Rinne: e', right positive, left negative. Schwabach: right normal, left positive. Hears much worse in a noise.
- (37) E. C., aged 50. Deafness and tinnitus for six years; can hear ordinary conversation at 2 ft., but is confused by shouting in ear; tympanic membranes normal; Eustachian tubes impervious to air per catheter. (Tested with eyes closed.) Rinne: e', right negative, left negative. Schwabach: right negative, left negative. Weber to right side. Acuity tests: air-conduction—Bezold-Edelmann: a, right -22 seconds, left -20 seconds; e', right -57 seconds, left -50 seconds; e'', right -25 seconds, left -20 seconds. Bone-conduction (meatus open): a, right -4 seconds, left normal; e', right -15 seconds, left -10 seconds; e'', right -5 seconds, left -5 seconds. Ipsilateral meatus closed: a, right -12 and -25 seconds, left -7 and -18 seconds; e', right -26 seconds, left -20 seconds; e'', right -16 seconds, left -16 seconds. Contralateral meatus closed: a, right -12 seconds, left -5 seconds.
- N.B.—The humming noise produced by inserting finger to close meatus would account for apparent prolongation of Schwabach.
- (38) Nurse K. Deafness associated with post-nasal catarrh and nasal polypi. Rinne negative, 5 seconds with Bezold-Edelmann e. Weber not referred. No loss of bone-conduction. Tympanic membranes intact. Hearing improves each time after catheterization, defect returning a few days later.
- (39) V. T., aged 30. Ménière symptom-complex; tympanic membranes normal; left side, hearing normal. Weber to left. Rinne: right negative. Acoumeter: right 0.3 m., left over 8 m.
- (40) C. M., aged 31, a lady's maid, under the care of Dr. Batten, with symptoms of extra-cerebellar tumour. First tested in July, 1911. Two years previously noticed tinnitus followed by deafness in the right ear, then numbness of right side of the face; three months later seen by an aurist and treated by Eustachian catheter inflations for several months. Patient felt sure this treatment was doing good; nevertheless, six months later attacked with dizziness, vomiting, and hemiparesis and hemianæsthesia right side of body. Hearing tests suggest defunct right eighth cranial nerve. Caloric tests: right negative, left positive. Rinne: right negative, left positive. Schwabach: right and left negative. Voice: right inaudible—e.g., shouting in right ear inaudible and large and small Edelmann whistles only faintly audible at maximum loudness when Bárány's noise apparatus is applied to left ear.
- (41) F. N., aged 60, under the care of Dr. Aldren Turner, for Ménière symptom-complex. Tympanic membranes intact. Rinne: e', right neutral, left +30 seconds. Schwabach: e', right -12 seconds, left -1 second. Weber to left.
- (42) C. O., complained of vertigo, deafness, tinnitus; can hear *tête-à-tête*; hearing is worse in a noise; tympanic membranes opaque, but intact. Rinne: e', positive. Schwabach: e', each side negative. Weber to right side.
- (43) T. P., aged 33, under the care of Dr. Batten, who referred patient for report on vestibular reactions, &c. History of deafness ten or twelve years; recently staggering gait; tympanic membranes, nose, pharynx, and Eustachian tubes normal. Rinne: e, right normal, left -10 seconds. Weber to right, but also audible in left. Schwabach: left -10 seconds. Rotation tests indicate diminished reflexes on left side.

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- (44) I. R., aged 56, under the care of Dr. Grainger Stewart. Progressive deafness for twenty years; "Quite deaf seven years"; severe tinnitus for three and a half years; "rushing noises" first noticed seven years ago; often giddy, never fell. Tested with every tone of the Bezold-Edelmann instruments. Left ear: hears the fork-tones from 36 d.v. to about 580 d.v., then with the whistles hears tones corresponding to a^1 (approximately 3,520 d.v.). In the right ear hears the fork 90 d.v., but no fork higher; hears whistles corresponding to tones e^2 and a^1 . Schwabach e , a , e^1 , a^1 , are each in turn heard momentarily at maximum amplitudes by bone-conduction in both ears; e^2 inaudible by bone-conduction. No tone on small Galton-Edelmann whistle audible.
- (45) T. S., aged 45, under the care of Dr. Farquhar Buzzard, with Ménière symptom-complex. Rinne positive, Schwabach negative, right and left. Weber to left side. Tympanic membranes and Eustachian tubes normal.
- (46) E. S., aged 33, under the care of Dr. Farquhar Buzzard, with typical Ménière symptoms. Tympanic membranes intact; partial nasal obstruction due to relatively enlarged turbinates; mucus in nasopharynx. Said to have been treated by an aurist without improving in giddiness. Rinne negative right and left. Schwabach positive right and left. Acoumeter: right 2 m., left 0-25 m.
- (47) E. S., aged 37, under the care of Dr. Grainger Stewart, with tinnitus, headache, and giddiness for three years, associated with deafness, which is always worse after head colds; tympanic membranes and Eustachian tubes normal. Rinne: e^1 , negative right and left. Schwabach positive right and left. Weber to left.

BRIEF NOTES OF CASES REFERRED TO IN CHART 10, SELECTED TO ILLUSTRATE TONE-RANGE, USING MONOCHORD FOR HIGH TONES AND BEZOLD-EDELMANN FORKS FOR LOW TONES.

- (1) S., adult male. Chronic otorrhoea right ear; tympanic membrane perforated antero-inferiorly; deafness slight. Weber to right. Rinne positive both sides.
- (2) B., a boy, with adenoids, recovering from recent middle-ear deafness, probably due to choked Eustachian tubes. Tested after inflation.
- (3) M., adult female. Tinnitus right ear, and slight conversational deafness following influenza several months previously. Weber to right. Rinne positive, right and left. Schwabach (Bezold-Edelmann's e fork): right and left - 3 seconds.
- (4) M., a young adult female, with chronic suppurative otitis media and attic cholesteatoma, left ear. Weber to left. Rinne: left negative, right normal.
- (5) T. T., a young adult male. Conversational deafness. Rinne positive. Weber neutral. Schwabach negative, especially right side. Bezold-Edelmann: e , - 5 seconds bone-conduction; e^1 , - 30 seconds air-conduction; e^2 , - 15 seconds air-conduction.
- (6) T., a married woman, aged 51, complaining of conversational deafness of three or four years' duration. Weak inflation sound per Eustachian catheter. Rinne neutral. Schwabach (Bezold-Edelmann e fork), - 3 seconds.
- (7) A medical man with commencing "hardness of hearing" in a noise and during general conversation, especially for high tones.
- (8) Mrs. S., aged 40. Deafness and tinnitus, chiefly right side, for over two years; tympanic membranes intact, and Eustachian tubes clear. Weber to right. Rinne, - 15 seconds. Schwabach, - 10 to 15 seconds, both sides (tested per auscultatory tube). Rinne: left + 17 seconds. Patient has attacks of giddiness and staggering; no headache.
- (9) R. S., a man, aged 55, with pain in mastoid region and partial deafness; was subject to earache in boyhood; fifteen months ago had bilateral acute otitis media and otorrhoea for two weeks; tympanic membranes intact; small opacity below umbo, left side. Stereoradiograms showed normal mastoid. Rinne: right + 25 seconds, left + 15 seconds. Schwabach: right - 25 seconds, left - 15 seconds.
- (10) H. S., a man, aged 60, with Ménière symptom-complex. Weber to right side. Rinne: right + 10 seconds, left - 7 seconds. Schwabach: right - 7 seconds, left - 10 seconds.
- (11) Mrs. S. Schwartze's operation left side nine years ago. Weber to left. Rinne negative both sides. Complaints of tinnitus and giddiness. Right tympanic membrane intact, left perforated inferiorly; inner tympanic wall nearly dry. Rotation tests normal.

- (12) Mrs. R. Normal hearing.
- (13) R., a young man, with Ménière symptom-complex and chronic suppurative otitis media, right ear; right membrane perforated antero-inferiorly. Labyrinth tests normal. Weber to right. Rinne: right negative, left positive.
- (14) M. R., aged 11. Recent Schwartz's operation right side for acute perforative otitis media with superficial mastoid abscess; tympanic membrane at time of testing healed. Weber to right. Rinne: right negative. Watch: 24 in. both sides.
- (15) Mrs. P., aged 62. "Hardness of hearing" for twenty years, chiefly right side, latterly left also, subject to severe head colds, which are followed by worse hearing; tinnitus like "threshing machine" in left ear. Rinne: right and left positive. Schwabach: right -5 seconds, left -2 seconds. Watch: right contact, left 1 in. Inflation of tympanum relieves tinnitus, but hearing tests remain unchanged.

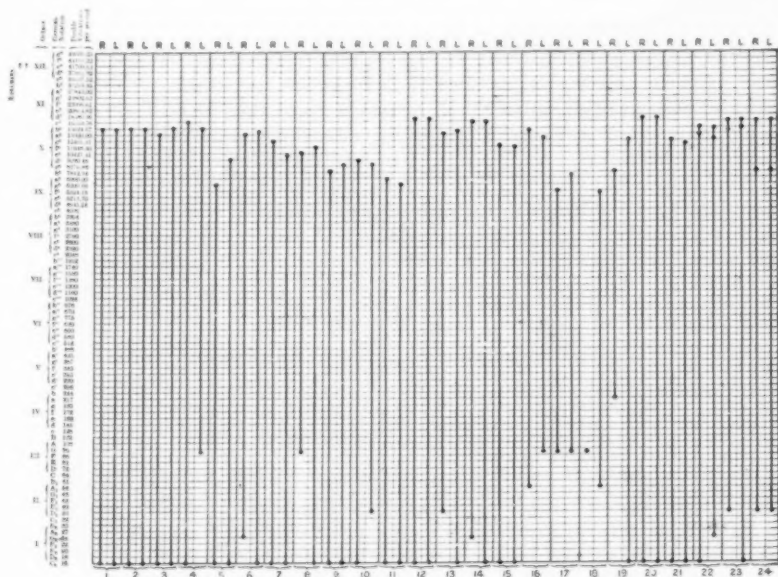


CHART X.

Table showing the tone-range in twenty-four intelligent patients, estimated by means of Bezold-Edelmann forks for the low tones and Van Struycken's steel monochord for the upper limit of tone-perception.

- (16) Mrs. M. Tinnitus and deafness after influenza twenty years ago; never otorrhoea or earache. Weber indefinite. Schwabach negative both sides. Rinne negative both sides.
- (17) Mrs. J., aged 60. Deafness for thirty-five years; recently worse after "influenzal" rhinitis. Weber to left. Rinne negative both sides. Schwabach negative both sides. Eustachian tubes patent (poltizerization).
- (18) Mr. H. Very deaf; cannot hear shout in right side; hears raised voice close to left side. Rinne and Schwabach negative both sides. Air-conduction: c³, left -18 seconds, right infinite loss, maximum amplitude. Watch nil. Exact upper tone-limit, right side, not ascertained, but below 5,000 d.v.

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- (19) Mr. H., aged 52. Right ear deaf after scarlet fever, when a student; otorrhœa many years; series of giddy attacks when aged 17, which culminated in severe "bilious attack" with vomiting and vertigo, for which he was confined to bed; subject to staggering for several weeks afterwards; since then never experienced giddiness nor sea-sickness; right tympanic membrane perforated inferiorly, and malleus fixed to inner tympanic wall; quite deaf to shout close to right ear when Bárány's noise apparatus is applied to the left ear. Weber's test indefinite, refers the sound to the head, not to either ear; this is the same whether the right or left or both ears are closed, and also whether the fork is applied to vertex or to either mastoid; the sound of the fork appears to be louder in the head when on the left mastoid than when on the right. Can hear Bezold-Edelmann forks when held to the right ear, by air conduction only when left ear is unstoppered. Bárány's noise apparatus excludes all tones from a to b², although these are referred to the right side when the left ear is open. Caloric tests: right side negative.
- (20) H. H. H., a boy, aged 11, with adenoids and imperfect hearing; improved by inflation. Before inflation low tone limit left side, 24 d.v.; after, 16 d.v. Rinne, -5 seconds both sides. Schwabach neutral.
- (21) T. F., aged 35, complaints of impaired hearing, tinnitus and dizziness of two or three years' duration. Weber to left. Rinne: right +25 seconds, left +15 seconds. Schwabach, -5 seconds on both sides. Eustachian tubes clear.
- (22) A. F., a boy, aged 14. Tested a week after acute non-perforative otitis media, left side; during acute attack the left tympanic membrane pale, bulging and pitting on pressure with probe. At the time of testing the swelling had subsided, and the malleus was visible. Weber to left. Rinne, left negative. Schwabach, left positive. Watch, 6 in.
- (23) Miss S., aged 32, noticed deafness, right ear, eighteen months; has habitually practised auto-inflation: right tympanic membrane "balloons" postero-superiorly; malleus does not appear to move. Weber to right. Rinne: right negative, left positive. Schwabach, -3 seconds both sides. Air-conduction: c⁴, right -4 seconds, left normal.
- (24) Miss H., an elderly nurse, who began to be deaf thirty years ago; uses a speaking trumpet; hears better in a noise; *l'été-à-tête* conversation heard fairly well; cannot hear the whisper; hears monochord up to 15 cm. by bone-conduction, but only up to 32 cm. by air-conduction; Eustachian tubes patent.

The PRESIDENT (Dr. W. Milligan) said the Section was infinitely indebted to Dr. Barr for his paper, and to Mr. Sydney Scott for his admirable and scientific demonstration. Mr. Scott had placed the subject in a way which was intelligible to all, and he (Dr. Milligan) at least had learned a great deal from it. One deduction he would make, partly from reading Dr. Barr's paper and partly from Mr. Scott's demonstration, was as to the desirability of those in that Section agreeing among themselves to standardize their methods of testing hearing; for instance, if all the hospitals in the United Kingdom were to use the same instruments and methods of testing, and were to record the results of such testings in the same way, a very valuable piece of work would have been done. There were so many methods in use that this lack of unanimity or uniformity was a detriment. The scientific demonstration which had just been given showed that much in this direction might be done from this time onwards.

(The discussion was adjourned until May 17.)

Otological Section.

May 17, 1912.

Mr. HUGH E. JONES, Vice-President of the Section, in the Chair.

Wax-plate Model of a Portion of the Labyrinth and the Inner Tympanic Wall in a Case of Post-suppurative Otitis Media.¹

By SYDNEY SCOTT, M.S.

THE patient was a man, aged 68, who died of malignant disease of the pancreas. For many years before death he had been "stone deaf" to "loud shouting into the ear."

The exhibitor received the right temporal bone in formalin (figs. 1 and 2), and found the tympanic membrane, malleus, and incus had disappeared, and that the tympanum, attic, aditus, and antrum were occupied by a small cholesteatomatous mass. There was no sign of granulation or pus.

The histological sections showed that the stapes and facial nerve were embedded in a mass of sub-cholesteatomatous fibrous tissue. The walls of the facial canal had been eroded and destroyed, exposing the nerve to pressure and displacement downwards, where it came into contact with the stapes. Both labyrinth windows were occluded. The stapes was perfect in all respects in every section. The cartilage cells in the base of the stapes and margins of the fenestra ovalis were unchanged, and the annular ligament was not thickened or displaced by bone. The vestibular nerve-endings were normal.²

¹ Shown at the meeting on March 15.

² Decalcification was carried out by the method previously described by author. The sections, embedded in paraffin, were cut with a flat-cutting Cambridge rocking microtome. All sections were mounted serially, and one in every eight was drawn by Edinger's projection apparatus, magnified 25 diameters, on to wax plates (2 mm. thick). (Born's method.)

[I desire to acknowledge my indebtedness to Mr. Walpole Champneys for his skilful assistance in assembling the plates, and to the Royal Society for a grant towards the expenses of the undertaking.—SYDNEY SCOTT.]



FIG. 1.

From outer aspect. 1, stapes; 2, facial nerve; 3, fossula rotunda and region of membrana secundaria, occluded by fibrous adhesions; 4, external semicircular canal (outer crus).

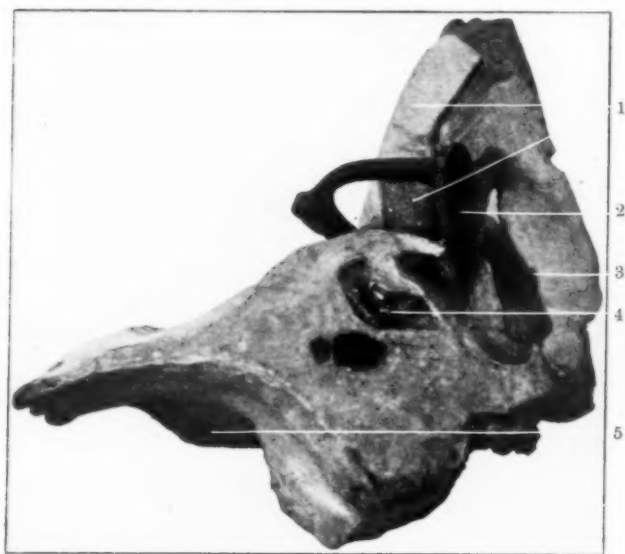


FIG. 2.

From upper aspect. 1, facial nerve; 2, stapes; 3, vestibule; 4, membrana secundaria and commencement of basal coil of cochlea; 5, jugular vault.

Discussion on the Value and Significance of Hearing Tests.¹

DR. DUNDAS GRANT expressed his gratitude to the authors of both papers. Dr. Barr's contribution embraced what was necessary for academic completeness, but those of his remarks which were based upon his own experience were well worthy of attention. In Mr. Sydney Scott's admirable and incalculably laborious and thoughtful work he made use of the charts originally devised by Hartmann, which were troublesome to calculate out in the case of each patient. He (Dr. Grant) had published what he called a "rapid method" of taking these charts, which he brought before the meeting of the British Medical Association in Edinburgh a number of years ago. With a series of tests with nine forks for the two ears it did not occupy more than about twenty minutes. He would be pleased to give particulars to any who might desire them. It was important to remember that tuning fork vibrations did not die down arithmetically, but geometrically. So that what Scott and Hartmann and he himself obtained by their tests was simply the percentage duration of hearing power, not the actual percentage of hearing power itself. To get that percentage of hearing power, if one went simply on the physical basis, calculating the dying down of the tuning fork, one got very different results. In fact, the tables gave in most cases a very much higher percentage of hearing power than the patient actually possessed. One had to remember, however, that one was dealing with something more than a physical element. Mr. Scott pointed out, in one of the most impressive paragraphs of his paper, that a very large psychical element came in which had not yet been calculated out. If one took a tuning fork and tried to listen to it dying away, he did not think it was possible to make the appreciation of such dying away agree with the physical curve. Probably the reason was that according to Flexner's law the gradual decrease was so attenuated that it could not be detected. He thought that in order to be perceptible there must be a certain percentage of difference; if it occurred in jumps, the tuning fork vibrations dying away would be detectable. Although the percentage duration was not an exact representation of the hearing power, it was so valuable clinically that for the present it would be foolish to throw it aside because it did not answer the theoretical standard.

¹ Adjourned from March 15.

With regard to bone-conduction, he asked why in the normal person that was less than air-conduction. The usual way of looking at it was that the air-conducting apparatus was such an excellent one, and so well adapted for its purpose, that nothing could be better. It was proved mathematically that it was a wonderfully constructed lever. On the other hand, the bone-conduction, which also seemed excellent, had to be conveyed through a heterogeneous medium. But that did not explain it all, and a very ingenious explanation had been offered by von Brünings, who said that in the normal person hearing by bone-conduction there was a combination of two methods of conduction—i.e., vibrations were conveyed though the bone directly to the labyrinth, but also through the conducting apparatus. That is, the air in the meatus and middle-ear was set in vibration at the same time. But it would be known from acoustics that when sound was conducted in two series of waves so that the heights and hollows of the vibration curves did not correspond, there was "interference" and the sound was deadened. That took place in bone-conduction, and therefore bone-conduction was not as good as air-conduction. In obstructive deafness when the tympanic arrangement was not working, this interfering element was eliminated, and therefore one found the bone-conduction, as tested otologically, actually greater in the patient than it was in the observer. Mr. Scott's explanation of the reflection of the waves was a very obvious one, and he did not doubt that, however ingenious the other was, this reflection was a very large element in the case. It was an extension of Mach's original view that the vibrations were prevented from escaping. Many years ago, he (Dr. Grant) observed that in a number of cases of simple ceruminous occlusion, where there was much deafness, the bone-conduction was not increased, as it was in a case of obstructive deafness arising from fixation of the tympanic apparatus. He thought it was a fair deduction that in order to get increased bone-conduction something more was required than mere closure of the meatus; one wanted elimination of the air-conducting apparatus—even for vibrations conveyed to that ear from the bone, and probably increase of tension.

With regard to Rinne's test, it was a very strange thing that in but few of the text-books was it laid down that a "negative" Rinne occurred in unilateral nerve-deafness. Each of the introducers of the discussion had referred to it, and he hoped it would be more recognized. In the *Transactions of the Otological Society*¹ he had himself published some diagrams illustrating the conveyance of sound to the labyrinth by bone-

¹ *Trans. Otol. Soc. Lond.*, 1901, ii, p. 63.

conduction, in which that was particularly dwelt upon. He christened it a "paradoxical negative Rinne." There was a point in Dr. Barr's paper with regard to positive Rinne which he had not been quite able to grasp. He saw no reason why the existence of nerve-deafness as such should make the Rinne test positive. It was not the existence of nerve-deafness which made it positive, it was the absence of obstructive deafness. And Dr. Barr mentioned cases of Rinne becoming positive from negative as an evidence that nerve-deafness had supervened. If that took place he would look upon it as a proof that the obstructive element in the deafness had disappeared. Another way of putting it was that the positive Rinne simply proved the absence of any such obstructive disease as would cause deafness. If deafness were present it must be accounted for in some other way than by obstructive disease, in fact by some form of nerve-deafness. One knew it was limited for practical purposes to the middle forks. The middle forks were those in which the logarithmic curve of decrement was most marked; and it was possible to have a sudden fall in vibrations of the tuning fork in the passage from the mastoid to the meatus, and thereby get a negative Rinne accidentally. He wished to mention a test which had been devised to find out whether a patient was conscious of hearing best in the midst of a noise. It was the outcome of the work of Sturm, who had sent a paper for publication in the *Journal of Laryngology*. The watch was put opposite the meatus, and drawn away until the patient no longer heard it, and then the vibrating tuning fork was placed on the mastoid. In cases of what might be called latent paracusis the watch was again heard by the patient at the distance at which it was not heard before. He had tried it in several cases and found it effective.

He hoped that the points he had mentioned were of some interest, supplementing but not in any way detracting from the value of the opening contributions.

Mr. MACLEOD YEARSLEY remarked that Dr. Dundas Grant had referred to the non-increase of bone-conduction in simple deafness from accumulations in the auditory meatus, and compared it with the increase of bone-conduction when the tympanic apparatus was interfered with. He (the speaker) asked whether that increase of bone-conduction in the latter case was not due to the better conducting power which occurred on account of the increase in tension in the tympanic conducting apparatus. He thought all the members would be very grateful to Dr. Barr and Mr. Scott for their papers, and he hoped that something practical would arise from them. He quite agreed with Dr. Barr that

the acoumetric formula which was suggested at the Budapest Conference of 1909 was very difficult to follow, and very complicated. He wished to propose that the Section should form a sub-committee to devise a formula for use in the Society, one which Fellows should use for recording their tuning fork and others tests when they brought cases before the Section. Otologists required in their work some means whereby they could arrive at a diagnosis in a large hospital clinic fairly quickly, and a simple formula to record the tests. Special cases of great interest could always be put aside for more careful testing afterwards. He thought such a formula should contain Weber's, Gellé's and Rinne's tests, a record of the bone-conduction, a record of hearing for low tones and for high tones, and a record of the hearing distance for the acoumeter, the ordinary voice and whispered speech. The tuning fork tests in that formula were helpful from a diagnostic point of view, and the tests with the voice and the acoumeter were useful as evidence of improvement. He asked whether Mr. Scott could say that the steel monochord was a reliable instrument for taking high tones. The ordinary Galton whistle he had discarded for some time, and had been using the Edelmann-Galton whistle, but he did not think this was above suspicion when used in the case of tones above 16,000 or 17,000 double vibrations per second. Moreover, the sound of the air passing through the whistle for very high tones added to the difficulty.

Mr. G. J. JENKINS expressed his appreciation of the opening paper, and especially of Mr. Scott's model. He thought, from an examination of the microscopic slides it would not be possible to reconstruct, but Mr. Scott had managed it. He had himself had some experience in the wax-plate reconstruction method of Born, and was able to appreciate Mr. Scott's work. The flattening out of the seventh nerve in that specimen was extraordinary, and he did not think anyone would have believed it possible unless one had seen the model, which gives absolute proof of the position and form of the nerve in this specimen. He understood that there had been a caries of the bony canal of the seventh nerve, and that cholesteatoma had flattened and pushed the seventh nerve down into relation with the stapes. From such a specimen one could more easily understand the relation of fibrous tissue to the stapes. He saw that fibrous tissue under the microscope, but would not be convinced that it was as Mr. Scott described it unless he could reproduce it in the model such as he had shown before this Section. This was a class of work which should be encouraged—namely, the reconstruction of deformities and pathological conditions. Dr. Barr made out the

Weber and Rinne tests to be somewhat in the nature of rivals, not as complementary. He had been making observations with the Rinne and Weber tests, and he had arrived at this conclusion: Observations and experiments made him believe that those tests were dependent, *first* on the fact that middle-ear deafness would, by interfering with the conduction of noises of an ordinary room diminish the confusion effect of those noises on the affected or more affected side; and so, when a sound stimulus was applied equally to both auditory terminals by placing a vibrating fork on the middle line of the head it would be appreciated more distinctly on the affected or more affected side; and *secondly*, on the localization and the source of a sound—a psychological process.

With regard to Mr. Scott's remarks on the comparison of air- and bone-conduction in the Rinne test, Mr. Jenkins did not think it could be held that this test implied that air-conduction was better than bone-conduction, but simply that the sound stimulus by air-conduction from the limbs of the fork was greater than the stimulus by bone-conduction from the base of the fork. Mr. Jenkins did not agree to the physics of Mr. Scott's theory by which he argued that bone-conduction was equal to or better than air-conduction. Mr. Jenkins thought it not altogether possible to compare the effect of the vibrations derived from the limbs of the fork (in air-conduction) with that of those of the base of the fork (in bone-conduction), as these vibrations were not the same. He said a tuning fork might be regarded as a bent rod clamped in its middle, which practically became a node. To the region of this node was attached the stem of the fork. When the limb of the fork was struck there were the coarse transverse vibrations which were the source of the sound vibrations by air-conduction of the Rinne test, but in addition there were longitudinal molecular vibrations set up by the above longitudinal vibrations, and these entered the base of the fork. There were, of course, some transverse vibrations going on in the base of the fork, but it was possible and probable that it was the finer molecular longitudinal vibrations which were taken up in bone-conduction. The form or degree of vibration might be suitable for establishing sound vibration in air, but not so for bone-conduction, and vice versa.

He was particularly interested in Mr. Scott's reference to the psychological side of hearing. There was still much to be done in that direction. With regard to acuity of hearing, he considered our instruments very imperfect, and he had tried to obtain help from various physics departments, but so far with little result. He was having some instruments made for trial. He thanked Mr. Scott for his splendid work on tone-appreciation in individuals suffering from nervous diseases.

Mr. WESTMACOTT seconded Mr. Yearsley's proposal with regard to a definite scheme of hearing tests. He had always felt it a great difficulty in a clinic to get through the tests in anything like a satisfactory way, both as to the time occupied, the difference in the instruments used, and the results obtained in different hands. He thought it would be a very fitting termination to this discussion if such a sub-committee could be appointed to draw up a shortened form of testing so as to eliminate those cases which did not require intricate and final tests. That would result in a convenient standardization for the purposes of comparison of results of testing.

The CHAIRMAN (Mr. Hugh E. Jones) said he was very much struck with Mr. Scott's remark about psychical deafness, as that was a matter which had always strongly impressed him. He had concluded that there were very many cases which were not deaf in the ordinary sense at all, and one could not find out that they were either nerve-deaf or deaf from defect of conduction, but they appeared to be psychically deaf. Perhaps it was impossible to prove that.

Mr. SYDNEY SCOTT, in replying on the discussion, expressed his regret that Dr. Barr was not present to answer for what he was responsible in his paper. In his own paper his object had been to put before the Section certain statements and suggestions to provide a basis for discussion. He laid stress upon two points: One was that he considered all tones were better conducted by bone than by air, and that he still maintained, in spite of what had been said in the discussion. It meant that reliance on Rinne's test was likely to lead to fallacies, and he thought on fuller consideration it would be agreed that he had good reasons for saying what he did. He did not know whether Mr. Jenkins's remarks had been rightly understood by him, but he hoped to read what he said, and then he might refer again to the subject. He expressed his appreciation of Dr. Dundas Grant's remarks, as well as Mr. Yearsley's. He was very appreciative of what Mr. Jenkins said, and particularly what he had done, because it was largely through his suggestions that the model which he (Mr. Scott) had reconstructed could be shown that day. Mr. Jenkins was the pioneer of wax-plate work in the Otological Section, and members would know his fine model of the human labyrinth, which he believed was the first one of the kind which had been produced in this country. Those who worked with the monochord would find that bone-conduction was better than air-conduction. He placed great reliance on the steel monochord, and agreed with Mr. Yearsley with regard to the Edelmann-Galton whistle.

The Semicircular Canals and the Sense of Position, or Orientation.

By DAN MCKENZIE, M.D.

SEVERAL years ago I used to attend an old lady who had lost her sight from glaucoma and a great part of her hearing from middle-ear and labyrinth disease. A sensation she used to complain very strongly of was that she easily lost her sense of position. She did not know, for example, after she had been in a room for some little time, whether she was sitting with her face to the window or to the door, and so on, and the bewilderment and confusion arising therefrom frequently gave rise to awkward mistakes and even accidents. This history was recalled to my memory about two years ago by a similar complaint that fell from a medical man, who had become absolutely deaf in both ears as a result of auditory nerve disease. His observation was that after being in his darkened bedroom for some time he lost his sense of orientation, and had to grope about to find some familiar objects of furniture before he was able to realize exactly where he stood. The experience was all the more remarkable in that it was new to him. Previous to the destruction of his hearing his sense of orientation had been unusually good, and he had been able to find his way about in fog or in darkness with extraordinary confidence and certainty. Casting about in my mind for an explanation of these symptoms, it occurred to me that the cause might lie in the interference with the vestibular organ which so frequently accompanies serious labyrinth or auditory nerve lesions, and the inquiry which forms the theme of this paper was the result.

The sense of position or orientation, in man, obviously depends upon sensations received not from one, but from several sense organs. The most important is undoubtedly vision; the next is, probably, the muscular or kinaesthetic (sensation of movement) sense—if we may call it a sense. (Occasionally hearing and even smell may be employed, but for ordinary purposes, in man, at all events, they may be neglected.) Knowing what we do of the vestibular sense and of its reflex effect upon muscle tonus, together with its preponderant influence, under normal conditions, upon equilibration, we might expect that vestibular stimuli, also, would add to the sum of impressions upon which is formed the

judgment as to our position relative to the outer world. In other words, arguing a priori, our sense of orientation, under normal conditions, must depend to some extent upon stimuli set up in the semicircular canals by turning movements of the head and body.

It would be well to remark, before going any further, that what is here termed the sense of position, or orientation, must be discriminated from equilibration or the maintenance of the body balance in all its many movements, which is, of course, very largely effected through the vestibular sense. In discussing orientation, or the sense of position, we are dealing with a function perhaps related to, but not to be identified with, that relating to equilibration. Certain observers go further than this, however. Cyon, for example, holds that orientation for near objects, which he refers to the vestibular sense, is inherently different from orientation for distant objects, and the latter he refers to other senses. That there is a difference between orientation for near and orientation for distant objects I agree, but surely it is a superficial and not an essential difference. In the case of near objects our judgment as to their position is founded upon sense-impressions from sight, touch, &c. And the same is true for distant objects, since the judgment as to their position relative to us is based upon sense-impressions of precisely the same nature. The fact that distant objects may be out of sight does not affect our judgment as to their relative position. Into the relationship between canalicular stimuli and our conceptions of space, the main thesis of Cyon's work, I do not propose to enter.

The question we are debating, then, may be enunciated as follows: Does the memory (conscious or subconscious registration) of turning movements influence the judgment in forming its conception of our orientation towards objects, near or distant? And if it does, are the direction and extent of the turning estimated by the vestibular sense as well as by the muscular sense?

Experiments bearing upon the problem of orientation in man have been variously devised and carried out from time to time, and the pointing test used in the diagnosis of certain nervous diseases is an instance of the application of those tests clinically. In labyrinth disorders, however, I am not aware of any experiments that have been tried in man, save those of Alexander and Bárány, and these were, for many reasons, imperfect.

Before proceeding to describe the experiments in man, I will first of all briefly touch upon the problem of orientation in animals.

ORIENTATION IN THE LOWER ANIMALS.

(I) *The Insecta.*

It is well known that animals show signs of possessing a more keenly developed sense of position than does man, or, at all events, civilized man. And it seems to exist in animals comparatively low in the scale. Bees, for example, are able to wing their flight for distances of two, three, and even four miles from the hive. The simplest explanation of their faculty for "homing" is that it is effected either through the agency of sight or of smell, or of both. Experiments with ants, also, have shown that these insects possess an accurate sense of their position relative to the nest, and this also some observers have attributed to olfaction.

(II) *Fish.*

The habits of fish are not sufficiently well known to enable us to estimate their powers of orientation precisely; but that fish do possess these powers is evident from such facts as that a salmon returns for spawning purposes to the river in which it was hatched.

(III) *Birds.*

Birds manifest a keener sense of position than any other animals. This is seen first of all in their migratory habits, and secondly in their homing instinct, the latter being, of course, a phase of the former. Birds are the most migratory of all animals. In Britain there are many wandering species, some leaving the island for the south in the autumn, others coming from countries farther to the north or east in order to winter in England. The journey from one abode to another sometimes occupies, it is said, as much as eighty or ninety days, and necessitates flight across seas like the Mediterranean or the North Sea. The course of their flight is not accidental or fortuitous, but, it would seem, bears evidence of determination and even of foresight. The subject has been studied in connexion with swifts and swallows, but so far without indicating the exact nature of the invisible thread that will draw from Algiers the same pair of swallows back to nest in the same window in the same English house, one year after another. Visual guidance, when we are dealing with journeys across the featureless ocean, is obviously out of the question, and so during flight is the muscular sense, and there are therefore only two other senses which require consideration. One is olfaction, the other is the sense of direction based upon past vestibular impressions.

In favour of olfaction is the often-recorded fact that land birds on their trans-oceanic flight will often perch about the rigging of a ship for several days; they leave the ship, however, before land is sighted, probably sensing the smell of the land in off-shore winds. On the other hand, although olfaction may be given a place in the scheme, it is unlikely that olfaction is the chief or only factor. Otherwise, a veering round of the wind when the birds are over the sea would remove their guide and leave them lost and helpless. Thus, by a process of exclusion, we are led to say that the birds must travel under some influence other than sight, olfaction, and the muscular sense, some sense-impression which is to them what the compass is to the sailor.

The same problem is even more distinctly seen in the case of the "homing" pigeon, and as this part of the subject has been investigated with some care, albeit so far without any definite or general agreement, it may be well to consider some of the theories which have been propounded to account for the instinct. Visual guidance undoubtedly plays a considerable rôle. This is evident from the fact that pigeons are not trusted by fanciers to find their way home if the distance is great, until they have been carefully trained, first by short and then by longer and longer flights, always in the same direction. That is to say, that if a flight of two or three hundred miles is to be accomplished, the birds are taken only a short distance from home to begin with. In subsequent training flights the distance is gradually lengthened until the requisite point has been reached. The necessity for such training clearly shows that, *when speed is required*, at all events, visual guidance is solely relied upon. Moreover, it is a fact familiar to pigeon-fanciers that if the weather is misty or foggy, the birds are very apt to lose their way; at all events, they do not return to the dovecot, or their return is delayed for several days. Thus vision is the most reliable guide for the homing pigeon. But is it the sole guide? Do circumstances ever arise in which the pigeon reaches home independently of things seen. Certain experimental results and considerations suggest, as in the case of migratory birds, that vision is not invariably the sole guide.

Thauziès has pointed out that when a pigeon is liberated some distance from a familiar landscape, it must soar to a great altitude before it can catch sight of a familiar landmark. But soaring does not occur. As a rule, after circling round the spot of liberation, the bird gradually makes a trend in the homeward direction, and then with some precipitancy finally disappears in that direction, flying a definite

and seldom interrupted course. In this connexion one of Schneider's experiments may be cited. He took a number of pigeons from home, some with the head and eyes covered, and others with the head uncovered, so that they could see the country they were passing through. All were, of course, uncovered when released. Curiously enough, it was found that the birds which reached home first were those whose heads had been covered on the outward journey. Schneider considers that his experiments favour exclusively the visual theory. But it is difficult to make the following result fit in with that theory. When he trained pigeons to fly in an E.N.E. direction and then liberated them at a spot E.N.E. of the dovecot, they flew E.N.E. on liberation and not W.S.W., as they ought to have done in order to reach home, and as they would have done had they depended solely upon vision.

Exner endeavoured to confuse pigeons by rotating them frequently on the outward journey and even by narcotizing them, but in spite of all his efforts the homeward journey was successfully accomplished. But he does not make it clear whether the journey was an old and familiar flight or not. It is obvious that sources of fallacy in experiments such as these must be very numerous, and should be carefully excluded.

Cyon thinks that the sense organ of orientation in birds is situated in the nose, but he does not seem to regard it as being olfactory in nature.

Finally, attempts have been made to settle the question by blinding pigeons or by destroying their semicircular canals. The attempts failed, however, because pigeons so mutilated cannot be induced to fly for any distance at all.

We are thus reduced to a condition of agnosticism so far as experimental results are concerned. It is probable that properly constituted experiments designed to test the various faculties in succession, and carefully guarded against fallacies, have never yet been performed. If homing depends upon a combination of sense-impressions, as is most likely, then conditions which render difficult visual guidance may not interfere with olfaction or the vestibular sense, and so on.

So far as the results go, they tend to show that (a) visual memories play an important part, but that (b) they do not play the sole part in directing the course to be flown.

Is there any direct evidence that the unknown sense which guides migratory birds across the seas and pigeons across unknown country is the vestibular sense? There is not. The great development of the semicircular canals in birds may be referred to the necessities of careful

balancing during flight. On the other hand, that there must be some unknown sense is certain, and that this unknown sense may be a finely organized vestibular system, as exquisitely developed as is the olfactory sense in dogs, is quite possible. On this assumption we can explain the general direction given to the birds' flight, like a captain who sets the course of his vessel, while as the bird nears familiar country and has to pick its way among particular details, sight and olfaction will supply the special direction of the flight, like a pilot who guides the vessel in and out among the shoals and currents of the home channels.

[Since the above was written I have been able, through the kindness of Mr. J. Lewis Bonhote, to obtain some recent information on the migration of birds, which is germane to the points we are considering. A considerable amount of work has been done by the late Herr Gätke on the Island of Heligoland, and the observations made by him and others show that in making their migratory flights the birds travel by night at a height often of 12,000 ft. above the earth's surface, and that they cover great distances in a single flight, even as far as from Africa to Heligoland. These facts, if facts they prove to be, are, of course, adverse to the theory of visual guidance. A series of experiments conducted by Professor John B. Watson, of Chicago, tend also to disprove the visual theory. Fifteen marked Noddies and Sooty Terns were taken from Bird Key, Tortugas, and released at distances varying from 20 to 850 statute miles. Thirteen of them returned to the Key, and among these were several birds which had been taken by steamer as far north as Cape Hatteras before being freed. The importance of this experiment may be estimated from the following circumstances: neither the Noddy nor the Sooty Tern ranges, as a rule, north of the Florida Keys. Thus the individuals tested had probably never been over the route before. Moreover, the route they were compelled to take excluded, it is said, the possibility of the guidance being effected by the wind. Finally, the absence of landmarks over the greater part of the journey rendered visual control an improbability.]

See *The Auk*, a quarterly journal of Ornithology, Cambridge, Mass., 1908, new series, vol. xxv, p. 333; and for recent work on Bird Migration, Thienemann, J., "X Jahresbericht (1910) der Vogelwarte Rossitten der deutschen ornithologischen Gesellschaft," *Journal für Ornithologie*, Leipzig, 1911, p. 620. Investigations are at present being conducted also by Mr. A. L. Thomson, of Aberdeen University, and Mr. H. F. Witherby, proprietor of *British Birds*, in Britain; C. C. Mortensen in Denmark, &c.]

We turn now to pedestrian animals. Experiments bearing upon the sense of orientation in rats have been carried out by Harvey Carr and John B. Watson. The animals were given the run of a small maze and the senses of smell and sight were eliminated. On shortening or on lengthening the runs of the maze, it was found that the rats overran the distance in the former, and made the turn too soon in the latter case. The movements were, therefore, guided by the memory of former muscular movements. On the function of the vestibular organ no light was thrown.

Domestic animals such as cats and dogs have often given surprising instances of the successful exercise of the homing instinct, and the same is true of horses. Many of these stories cannot be explained save on the assumption of the existence of some sense much more acute than man possesses.

ORIENTATION IN MAN.

Most people will agree that the powers of orientation vary very much in degree in normal human individuals. And this is borne out by my experiments. Further, as far as conscious self-analysis is concerned, the sense of position would seem to depend upon the results of a combination of visual, tactile (or kinæsthetic), and perhaps also vestibular impressions. That we rely largely, and even in some people exclusively, upon visual observation is proved by the familiar fact that in places where a sameness of visual objects occurs (in Tube stations, circular rooms, &c.), we readily lose our sense of position, the loss being accompanied by a curious feeling of detachment and bewilderment almost amounting to vertigo. At the same time there are many individuals, even in civilized communities, whose sense of position is almost or entirely independent of vision. Such people are seldom or never at a loss even in strange localities, and at night or in fog and mist.

To turn now to the experiments bearing upon the sense of position in man. The object I had in my mind was to ascertain, if possible, whether or not the vestibular organs exercise any influence upon our sense of position. The difficulty was to devise an experiment which would exclude, or minimize, the influence of the other senses, and more particularly the muscular sense. We have already seen that the muscular sense must be at its lowest point of activity in the flying of birds, and the nearest approach to birds' flight in the case of a man is the act of swimming. In this connexion James's interesting statement may be recalled, as to the difficulty deaf-mutes experience in

orientating when swimming under water. The experiment of blind-folding deaf-mutes in whom the vestibular sense is inactive should be repeated, as doubt has been thrown upon James's statement. In swimming, stimuli from tactile and kinæsthetic sources must be practically in abeyance, and I imagine that swimming experiments upon deaf-mutes would be crucial so far as information upon the part played by the vestibular organs in orientation is concerned. Experiments such as these being inapplicable, I carried some out upon people standing and walking, and in them, therefore, the muscle sense could not be eliminated. But by testing people in whom rotation and the caloric tests showed the vestibular sense to be defective or absent, and comparing them with the normal, I tried to determine whether or not the muscle sense was influenced by sensations derived from the semicircular canals.

The experiments are carried out as follows: A large quiet room is selected and the subject, carefully blindfolded, is made to advance to an object placed 16 ft. in front of him, and the deviation to one or other side is noted. (The normal shortness of one leg compared with the other is insufficient to interfere with the test.) The subject then returns to the original standing place and is made to execute turning movements, and after each turn he again walks toward the distant object, and the deviations are noted. Thus he takes a quarter, a half, and a complete turn to the right and to the left respectively. Having examined a number of normal individuals in this way, I proceeded to carry out the same experiments upon people in whom the usual tests showed the vestibular system to be more or less impaired. Twenty-two people in all were tested—nine normal, nine with an impaired vestibular system, and four in whom no response to the vestibular tests could be evoked. The results were not altogether definite, as might perhaps have been expected. To begin with, considerable variation was found in normal individuals. After complete turns, for example (executed slowly so as to avoid vertigo), deviations of 4, 12 and even 18 ft. were noted. People with a naturally keen sense of direction responded most accurately. Variations in the same individual at different times were also found, but not to any very striking extent. In people whose vestibular system was impaired, but not altogether inactive, a similar latitude of variation was found, but these people, almost without exception, showed wider deviations than normal individuals did, and several were incapable of making complete turns. In the four patients with entire absence of vestibular response and,

of course, with complete deafness, one showed considerable deviation (20 ft. to right after "complete turn" to left, and 14 ft. to left after "complete turn" to right), but two of the others responded like normal individuals, very much to my surprise.

The number tested is, of course, too scanty to permit of anything more than an impression. But the difference between the "normal" and the "impaired" cases is, I think, sufficiently striking to justify us in holding that canalicular stimuli do influence our sense of position. It is probable, however, from my results in cases with absence of vestibular response, that these stimuli are dispensable and that the nervous system can accustom itself to their absence. The great errors made by patients with "impaired" vestibular reaction may possibly be due to the passage of irregular stimuli from the canals to the nerve-centres. It is obvious that the moment when stimuli from the canals will chiefly be relied upon will be when the subject is sitting or lying still with closed eyes. In normal individuals the constant or almost constant flow of stimuli from the canals will on such occasions serve to keep the sense of orientation awake or active. But in people with defective or absent vestibular systems the absence of this constant and regular stimulus, slight though it may be, will, when the visual and kinaesthetic sensations are in abeyance, produce the sense of bewilderment or confusion which attends the loss of orientation. In this way we may explain the symptom experienced by Mr. Macleod Yearsley's case reported in the *Lancet* of February 17, 1912, as well as of the feeling of loss of the sense of position in the two cases I alluded to in the introduction to this paper. Obviously, the symptom may be found in cases both of complete and incomplete vestibular destruction, but in the former it will probably tend to disappear.

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TESTS FOR ORIENTATION.

Three typical instances.

(I) NORMAL INDIVIDUAL.

Direction						Result
Straight forward	2 ft. to left
Quarter turn to left	3 ft. "
Half	Correct
One	4 ft. to left
Quarter	...	right	Correct
Half	8 ft. to right
One	16 ft. "

(Some sense of confusion at end.)

(II) INDIVIDUAL WITH IMPAIRED VESTIBULAR REACTIONS.

Straight	10 ft. to left
Quarter turn to left	10 ft. "
Half	? confused
One	(shown)	Correct
Quarter	...	right	14 ft. to left
Half	Correct
One	60 ft. to left

(III) INDIVIDUAL WITH ABSENCE OF VESTIBULAR REACTIONS.

Straight	4 ft. to right
Quarter turn to left	18 ft. to left
Half	3 ft. "
One	20 ft. to right
Quarter	...	right	6 ft. to left
Half	8 ft. to right
One	14 ft. to left

ANALYSIS OF RESULTS.

Straight Forward.(A) *Normal*.—Three correct, six deviated; average extent of deviation = $2\frac{1}{2}$ ft. to left, $1\frac{1}{2}$ ft. to right.(B) *Impaired Vestibule*.—Two correct, seven deviated; average deviation = 6 ft. to left, 3 ft. to right.(C) *Vestibule Inert*.—Two correct, two deviated; average deviation = 1 ft. to left, 4 ft. to right.*Quarter Turn to Left.*(A) *Normal*.—Two correct, seven deviated; average deviation = $3\frac{1}{2}$ ft. to left, $2\frac{1}{2}$ ft. to right.(B) *Impaired Vestibule*.—Four correct, five deviated; average deviation = 11 ft. to left, 9 ft. to right.(C) *Vestibule Inert*.—One correct, three deviated; average deviation = $7\frac{1}{2}$ ft. to left.

Half Turn to Left.

- (A) *Normal*.—Three correct, six deviated; average deviation = $3\frac{1}{2}$ ft. to left.
 (B) *Impaired Vestibule*.—One correct, six deviated, two failed to make the turn; average deviation = 12 ft. to left, 14 ft. to right.
 (C) *Vestibule Inert*.—Four deviated; average deviation, 11 ft. to left.

One Turn to Left.

- (A) *Normal* (one lost).—One correct, seven deviated; average deviation = $3\frac{1}{2}$ ft. to left, 12 ft. to right.
 (B) *Impaired Vestibule*.—One correct, three failed to make the turn, five deviated; average deviation = 13 ft. to left, 14 ft. to right.
 (C) *Vestibule Inert*.—One failed to make the turn, three deviated; average deviation = 2 ft. to left, $10\frac{1}{2}$ ft. to right.

Quarter Turn to Right.

- (A) *Normal*.—Two correct, seven deviated; average deviation = 3 ft. to left, $2\frac{1}{2}$ ft. to right.
 (B) *Impaired Vestibule* (one lost).—One correct, seven deviated; average deviation = 11 ft. to left, 5 ft. to right.
 (C) *Vestibule Inert*.—Two correct, two deviated; average deviation = $4\frac{1}{2}$ ft. to left.

Half Turn to Right.

- (A) *Normal*.—Two correct, seven deviated; average deviation = 3 ft. to left, $9\frac{1}{2}$ ft. to right.
 (B) *Impaired Vestibule* (one lost).—Two correct, six deviated; average deviation = 8 ft. to left, 19 ft. to right.
 (C) *Vestibule Inert*.—One correct, three deviated; average deviation = $9\frac{1}{2}$ ft. to left, 8 ft. to right.

One Turn to Right.

- (A) *Normal* (one lost).—None correct, eight deviated; average deviation = 10 ft. to left, 15 ft. to right.
 (B) *Impaired Vestibule*.—None correct, four failed to make the turn, five deviated; average deviation = 35 ft. to left, 6 ft. to right.
 (C) *Vestibule Inert*.—None correct, four deviated; average deviation = 10 ft. to left, 15 ft. to right.

N.B.—All the "normal" cases made complete turns. In 14 per cent. of instances an incomplete turn was made in "impaired" cases. In 3.6 per cent. of instances an incomplete turn was made in "inert" cases.

The average amount of total deviation was: In "normal" cases, 5 ft. (circa); in "impaired" cases, 12 ft. (circa); in "inert" cases, 7 ft. (circa).

DISCUSSION.

Professor PRITCHARD said it was now thirty-five years since he was first interested in this subject by a practical experience. Four pedestrians, of whom he was one, lost their way in a mountain cloud. Three of them were brothers. A compass was used to get the direction, and it proved to be the opposite to what each thought it to be. They fixed their direction and walked on, and then fixed it again. All the three brothers worked round to the right, and the fourth worked to the left; and that was done over and over again. The experiment was an advantage in that it was light, and yet sight played no part. He felt certain it was vestibular, and it showed that all persons were not equally balanced in the matter of orientation; there was a tendency to go either to one side or the other. It explained the fact that a man when lost in the bush usually went round in a circle. He was much interested in Dr. McKenzie's contribution, and if what he said was correct, the birds alluded to were much better off than human beings in their sense of position.

Mr. MACLEOD YEARSLEY alluded to a paper recently read before the Neurological Section by Dr. Golla,¹ who had been doing a series of experiments on space perception in man. The author and he did some of those experiments upon congenitally deaf children, and upon some totally deaf children who owed their deafness to congenital syphilis. Their conclusions were somewhat indefinite, because the results of the experiments, like those of Dr. McKenzie, were not very definite. But in some ways the results were rather surprising, because some of the children, who could not be made giddy on a turntable, although spun round for a quarter of an hour, were able to walk blindfold straight across the hall, a distance of about thirty yards. With regard to orientation in lower animals, he did not see any reference in Dr. McKenzie's paper to the accurate work of Dr. Forel, who some years ago published a number of experiments of his own on the homing instincts of birds, bees, and ants. He had shown to his own satisfaction that the homing instincts of bees are probably due to the sense of sight, and in ants to their antennary sense. He believed that homing pigeons orientated themselves largely by sight, and he instanced the experiments of Cyon, who carried pigeons to a distance of 70 kilometres. Some of these pigeons had their ears closed with collodion and wool, and others had the nose similarly occluded. Those with the closed ears returned first, and those with the closed noses were four days longer, and only returned when the collodion disappeared. By this means he concluded that homing pigeons got home by means of smell. Forel maintained that pigeons orientated themselves by the sense of sight, and said that the terrestrial creatures like ourselves had no conception of the enormous field of vision which birds must have. Now that man had taken to aeroplaning he might be better able to appreciate this. Dr. McKenzie did not seem to believe much in the theory of visual guidance, and he did not know whether he had reflected upon the tremendous field of vision possessed by a bird flying thousands of feet above

¹ *Proceedings (Neur. Sect.)*, pp. 123-36.

the surface of the earth. It was well known that vultures seemed to appear from nowhere when there was carrion in the desert, or there had been a battle, and those who had watched seabirds fishing would appreciate the keenness of their sight.

Dr. H. J. DAVIS said he was much interested in the passages in the paper dealing with orientation in fish. It seemed to be that the lower down in the animal scale one went the better was the orientation. The salmon was low in the scale, but as was pointed out, it would return for spawning purposes to the place where it was hatched. Salmon not only found again the estuary of the main river in which they were born, but they would re-traverse the same river and the same tributary of that river to get there; and they were said never to go beyond the spawning bed on which they were hatched. It was found that some salmon did not return every year to spawn, but only every third, fourth, or even fifth year, and yet they would go up the same stream to do so. It was said that they judged largely by the temperature of the water, but as that was not uniform at the same time of the year he did not agree with that. Mr. Hutton had done some remarkable work by microscopic examination of the scales of salmon in the Welsh Wye River, and he could ascertain thereby the age of a fish and say whether it had spawned or not, and also when. He did not see how the accuracy of the return of the fish could have anything to do with the semicircular canals; the fish must have some instinct which humans have not. Darwin, he thought it was, related the story of a man who had retained some wild geese which, with one exception, were allowed to escape at the migration season. The wings of one bird were clipped, and it then was allowed to escape, and it was found afterwards tramping down the road in the same direction as that in which the others had flown.

Mr. WAGGETT said he would like to know what the authorities had to say with reference to the sense of the north, which was very definite in some, but was not common to all. He had himself an innate knowledge of the north perfectly well defined, except when he was out of health. He assumed that pigeons possessed that sense more keenly than human beings. His impression was that many of the sensations upon which men relied in their daily life were things which had not been analysed and which were not yet understood.

Dr. DUNDAS GRANT considered that the paper was to be commended in many ways, and particularly for the frankness and honesty with which the author had detailed the results of his experiments. Those experiments might support certain views, but he had not tried to make too much of them. He hoped Dr. McKenzie would be induced to carry his work further. In the cases where deviations had taken place, he asked whether he meant one vestibule was impaired, or both. Most of the people who were tested deviated to the left, and that he (the speaker) considered a physiological condition. There were some people who could sleep east and west, but who felt they could not sleep north and south. Birds might have the same sensitiveness to the earth's magnetism. With regard to whether animals possessed senses which we did

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not, or whether certain senses in them were more highly developed, it seemed to have been made out by the discussion that homing birds had an enormously wider range of vision than man, and the comparison was something like that of the geography of a child born and living in a poor part of London compared with that of a man owning a motor car who made considerable use of it. Snails possessed the capacity of knowing of the presence of another sympathetic member of their species at a considerable distance, even if enclosed in a box. No doubt the vestibular sense helped in so far as it indicated changes of movement or position on the part of the individual—his orientation—but its share in the choice of direction in migration could be only a small one.

The CHAIRMAN (Mr. Hugh E. Jones) asked whether Dr. McKenzie considered, as the result of his experiments, that the complete ablation of the semicircular canals brought one back nearly to the original state—i.e., whether he had made a marked distinction between impairment and ablation. Must one consider that ablation was not a serious injury? He took it that in cases of impairment, confused stimuli were sent up to the centre for orientation, whereas when the canals were completely absent there were no stimuli at all, and the judgment was not interfered with. Could members console themselves when they had ablated a labyrinth that they had not deprived the patient of an essential organ?

Dr. McKENZIE, in reply, said most of the points which had been raised would be found to have been answered in the paper. The question of space perception was another chapter in the same subject. He did not agree with Cyon that the whole of our idea of space perception was dependent on the canals; he believed sight had much to do with it. Mr. Yearsley's experience with children with vertigo was borne out by his own experiments, and that answered the Chairman's question about ablation. He believed that ablation removed abnormal stimuli, and orientation by vision and also by the muscular sense became extraordinarily perfected. In that way the person was able to dispense with the labyrinth. The sense of the position of "the north" was another way of expressing the sense of orientation, and it no doubt depended largely on the points he had touched on in the paper. When he referred to "ablation" of the labyrinth or "impairment" of it, he meant both labyrinths.

The Voice-raising Test with Bárány's Noise Machine.

By J. DUNDAS GRANT, M.D.

DR. GRANT showed a patient with complete bilateral deafness on whom he demonstrated the effect of Bárány's noise machine. In the case of Fellows of the Section with normal hearing, the application of the machine to either ear during the process of their reading aloud

resulted in a great increase of loudness of the voice during such application, the reader being quite unaware of any change of effort. On the other hand, the application of the machine to the deaf patient produced no alteration in loudness during reading. It was an admirable means of testing for malingering, as it would be practically impossible to simulate the effect. In a case of unilateral deafness the voice-raising was distinctly greater when the noise machine was applied to the good ear than when applied to the deaf one, in the latter case it being almost *nil*.

Notes of a Case of Deafness caused by Excessive Tea-drinking.

By ALEXANDER SHARP, F.R.C.S.

A. E., FEMALE, aged 40, complained of increasing deafness for about eighteen months. On examination: Difficulty in locating sound; no tinnitus; watch and whispered voice heard about 6 in. from both ears; nose and throat healthy; tympanic membranes normal. Tuning fork tests typical of nerve-deafness. Family history negative. No syphilis. Patient is engaged in business which gives her a good deal of worry. She finds that strong tea cheers her up, and admits to taking it as often as eight or ten times a day. Tea-drinking stopped, and in four weeks hearing improved to 18 in. for watch and whispered voice. Improvement continued until hearing was nearly normal. In spite of warning patient again took to tea-drinking and deafness resulted. On again giving up the habit normal hearing returned.

Mr. MACLEOD YEARSLEY regarded the case as a very interesting one, and he had come across nothing similar in otological literature. He asked whether the tea was made fresh, or whether it had been stewing for some time, as some women liked it. An interesting point in this connexion was that a large amount of tea was drunk by people in Australia, by some at almost every meal in the day, yet one never heard of tea-deafness in that country. He asked whether there was any particular poison in the tea which would act on the internal ear. Also, he would like to know what the tuning-fork tests were; they were said to have been typical of nerve-deafness. Was there any loss for high tones? It looked as if there was toxæmic deafness which got well.

A Case of Raynaud's Disease, with Vascular Disturbances in the Labyrinth.

By H. J. DAVIS, M.B.

THE patient is a married woman, aged 51; she has been attending the electrical department under Dr. McDougal for several months with well-marked, though not advanced, Raynaud's disease. Both hands are affected. Her condition has much improved with treatment.

During the last three months the left ear has become affected, and the auricle presents some of the usual signs characteristic of the disease; but what troubles the patient most is a violent tinnitus with giddiness coming on "with a sensation of burning heat in the ear." This tinnitus ceases suddenly, as a rule, when in bed, and "the inside of the ear then becomes so intensely cold that she feels as though there was a piece of ice inside the ear." This sensation slowly passes off. "The hearing is not affected except when the noises come on." The tinnitus is evidently due to disturbances in the labyrinthine circulation.

The patient, a very nervous woman, has been much improved by a mixture of hydrobromic acid and nux vomica, to which 10 gr. of calcium lactate have been added for each dose; this she has taken for a month. No electrical aural treatment has been applied.

DISCUSSION.

Dr. DAVIS, in reply to questions, said the tinnitus was not of the pulsating character, and the fields of vision had not been tested. She was very difficult to interrogate because she became so very nervous and giddy.

Dr. GRANT pointed out that where the tinnitus was pulsating, it could often be stopped by digital compression of the carotid arteries and the vertebral arteries behind the neck. He showed his method of compressing the vertebral arteries.

The CHAIRMAN (Mr. Hugh E. Jones) did not think the deafness passing away when she lay down accorded with hyperæmia of the labyrinth.

Otological Section.

June 8, 1912.¹

Dr. W. MILLIGAN, President of the Section, in the Chair.

The Value of Radiography in the Detection of Mastoid Disease.

By A. E. BARCLAY, M.D., and W. MILLIGAN, M.D.

IN the majority of cases of mastoid suppuration there is little doubt as to the diagnosis at the time when the surgeon operates, and the condition found at operation almost always justifies the inference deduced from the clinical signs. It is, however, only when suppuration is well established that the disease can be diagnosed with certainty. While waiting for reassuring evidence on which to explore the mastoid cells the patient is subject to very definite risks. The possible spread of infection to the cranial cavity is a danger so grave and so serious that some surgeons feel bound to operate in doubtful cases rather than await the advent of absolutely definite evidence. This course doubtless involves less risk to the patient, but it not infrequently happens that an unnecessary and serious operation is undertaken by those surgeons who are willing to hazard their own reputation as diagnosticians rather than to submit the patient to the dangers of delay. Again, there are cases in which a local external lesion masks disease of the mastoid cells. In such cases some surgeons prefer to deal with the external condition and then to await developments, a procedure which often necessitates a subsequent exploration of the mastoid cells which might as well have been undertaken when the primary operation was performed. If definite evidence could be obtained in such cases the surgeon could confidently recommend the performance or the postponement of an operation and so be freed from an anxiety which has sometimes driven

¹ Extra-Metropolitan meeting, held at The Royal Infirmary, Manchester.

him to operate in spite of the absence of definite clinical signs, with the result that he has been disappointed and has perhaps failed to explore in a subsequent case until too late, with disastrous consequences. It is with the object of determining the value of an X-ray examination in the doubtful rather than in the straightforward cases that we have undertaken this investigation.

There is a tendency in nearly every department of hospital work to rely too much on X-ray evidence and to take the dictum of the radiographic evidence as the last word in diagnosis. This is by no means an unmixed blessing, for it leads to slovenly clinical work and a dependence on technical aid which is available only in the larger hospitals. Even if radiography should turn out to be of great assistance in the diagnosis of these difficult cases we would, at the outset, emphasize the necessity of a detailed clinical investigation before resorting to radiography. Should radiography eventually achieve a complete triumph—which does not seem at all likely—we would ask you to let radiography be the last word by all means, but not also the first and only means of investigation employed.

The theory of these examinations is quite simple. Two radiographs of the head are taken, one from each side, the essential point being that the head should be firmly fixed in precisely the same relative position for the two plates so that an exact comparison may be made when the negatives are developed. We have tried a variety of positions in order to show the mastoid cells more clearly, and find that the best results are obtained with the X-ray tube centred an inch above the external auditory meatus. This Section will not be interested in technical details which are rather the province of the radiologist than of the otologist; suffice it to say that only the best negatives will be of value, and even so they must be examined under the most favourable conditions. Some form of viewing box which enables an examination of both plates at the same time is necessary; and it goes without saying that the person who examines the plates should do it with an open mind, preferably not knowing on which side the disease is suspected, for in many of the cases the changes seen are quite slight and any preconceived ideas are a hindrance rather than a gain. No attempt should be made to form an opinion until after the plates are dried, as a wet negative reveals far less detail than can be detected on the dried plate.

Any air space within the bone allows the X-rays to pass through more easily than through the bone itself, hence the air spaces in the

mastoid process should show up as comparatively dark areas on the negative, while any filling up of the cells with pus will lead to their obliteration. The presence of a thickened mucous membrane will decrease the translucency without actually obliterating the outline, with the result that although the presence of the air cells can be detected they are indefinite in outline and very hazy. The method of examination is quite simple in theory but in practice there are many difficulties. In the first place, only the most perfect plates are of any value, and to obtain a pair of the most perfect plates is not easy in this region owing to the density of the brain and skull. Moreover, the patient's head must be held absolutely still during the exposure, and this is often next to impossible owing to the pain produced by attempting to fix the head, and partly no doubt also to the dull mental condition usually present—the result of deafness and disease. These, however, are technical difficulties which the radiographer should be able to overcome if he has a sufficiently powerful apparatus at his disposal to obtain rapid exposures.

The human frame is not all turned out from one mould, and the mastoid cells are exceedingly variable both in size and number. Fortunately, however, they seem to bear a certain resemblance on the two sides, and so far as we have been able to judge there is seldom any marked difference. If, therefore, we have plates of the two sides for comparison we should be able to form an opinion as to the translucency of the cells. We have found that in children the cells occupy a much larger proportion of the mastoid process than in adults, also that the actual radiography is an easier task, although it is more difficult to maintain fixation of the head, so that, apart from technical difficulties, it should be easier in young subjects to form an opinion.

Another source of error in diagnosis arises from the fact that the presence of old-standing disease tends not only to thickening of the mucous membrane but also to sclerosis of the mastoid trabeculæ, a sclerosis which we have noted in some cases to exist from base to apex.

To commence an investigation with a preconceived idea based on isolated cases is most unwise, and in order to avoid this we have simply set aside all our material for this communication and have not attempted to draw any conclusions until we came to the compilation of this paper. The X-ray negatives were then carefully examined without reference to the notes and the reports were drawn up in entire ignorance of the condition found at the operation, but with the experience we had previously obtained.

We will now briefly review some of the cases, for the notes of which we are indebted to Dr. Diggle (House Surgeon to the Throat and Ear Department):—

Case I.—A woman, aged 40, who had suffered from otorrhœa since childhood up till two years previously. Five days before admission she complained of earache, and on admission there was tenderness and œdema over the mastoid. The temperature was 103° F., and the pulse 120. There was no nystagmus; Kernig's sign was present; there was no head retraction; vertigo was marked. The cerebrospinal fluid was not under tension, but it was turbid. The radiograph showed that the cells on the affected side were completely obliterated, as you will see on the lantern slide. At the operation a suppurating cholesteatoma in the antrum and a labyrinthine fistula were found. There was no sinus thrombosis. A complete post-aural operation was performed. In this case the radiographic evidence was quite definite and pointed to complete obliteration of the cells, a condition which was entirely in accord with the operative findings.

Case II.—A youth, aged 17, who had recently suffered from influenza; for three weeks he had suffered from otorrhœa. A subperiosteal mastoid abscess was present and was incised, and it was after this procedure that the radiographs were taken. The plates showed distinct haziness of the mastoid cells, but that they were not completely obliterated. The exploration of the mastoid revealed the presence of pus in the antrum. In this case the radiographic evidence was not definite. It suggested rather a thickening of the mucous membrane than the presence of actual pus in the mastoid.

Case III.—A child, aged 8, in whom a subperiosteal abscess was present. The radiograph of the affected side showed the mastoid cells clearly. There was no obliteration or haziness of the outlines. The abscess was incised, and two days later the mastoid was explored and found to be quite healthy. In this case, therefore, the radiograph gave a true indication of the condition of the cells, and if at the time we could have relied upon the radiographic evidence it would have saved an unnecessary operation.

Case IV.—A boy, aged 4, who had suffered from chronic otorrhœa for several years. He suffered from vertigo and there was a perforation of the membrana tympani in its anterior segment. The radiographs showed that the cells were ill defined and very hazy, but not obliterated completely, and an exploratory operation showed that there was no recent pus in the antrum, but that the mucous membrane was thickened.

Case V.—In the next case the X-ray plates gave evidence which was very similar to that in the last case quoted, and the lantern slide might be from either of them. The patient, a girl, aged 21, gave a history of otorrhœa of several years' standing and a condition of chronic post-scarlatinal otitis media was diagnosed. There was slight facial paralysis; no vertigo and no nystagmus. As you see, there is definite haziness but not complete obliteration of the cells on the left side—the affected side—while on the right side the

cells appear to be quite healthy. A complete post-aural operation showed that there was no pus in the antrum at the time of the operation, but that the mucous membrane was unhealthy and thickened.

Case VI.—A man, aged 28, who had had earache and otorrhœa for five weeks. There was tenderness and œdema over the mastoid apex and upper part of the neck, but there was no nystagmus or vertigo. The blood count showed a marked leucocytosis (14,800). The radiographic evidence showed that the cells on the affected side (left) were completely obliterated, but those on the right side were apparently quite healthy. It was found that the mastoid cells and antrum were filled with pus and that there was a perforation of the apex on the inner side. The dura mater of the posterior fossa was exposed. The radiograph of the unaffected side, which you see, shows a series of cells placed very closely along the upper and posterior margin of the mastoid process, indicating, perhaps, the thin layer of bone which separates these cells from the cranial cavity. Presuming that the formation of the two sides is symmetrical, one is perhaps justified in reading the X-ray evidence of obliteration of the cells in this case as of far greater importance than in the other cases, since there is so thin a layer of bone separating the obliterated cells from the cranial cavity.

Case VII.—A child, aged 2, with right-sided otorrhœa of indefinite duration. There was a mass of suppurating glands in the neck and an abscess over the mastoid. The blood count gave a leucocytosis of 14,500. The radiographs showed that the cells on the right side were obliterated and that on the left side they were distinctly hazy. The right side was treated by removal of the glands, incision of the abscess, and paracentesis, which proved sufficient, as the discharge ceased and the leucocyte count fell to 7,500. Within a few days the left ear began to give trouble and a discharge was noted, but this also was cured by paracentesis, although the leucocyte count rose to 15,000 several days after the paracentesis. It seems probable, therefore, that the radiographs indicated the presence of pus within the cells on the right side and that on the left there was, at the time the radiographs were taken, at the most a thickening of the mucous membrane which may or may not later on have given rise to an accumulation of pus within the cells. This case goes far towards proving that in children at any rate actual mastoid suppuration may clear up without any other treatment than paracentesis.

Case VIII.—A woman, aged 36, who had suffered from pain in the right ear for three weeks. There was some otorrhœa and tenderness over the mastoid. There was no history of previous trouble. The radiographs suggested that the cells on the right side were quite healthy but that they were obliterated on the left side. An exploratory mastoid operation showed that there was no pus in the mastoid cells on the right side and that the whole trouble was due to furunculosis of the meatus. The radiograph of the affected side gave correct information as to the condition of the cells, but we are at a loss to account for the obliteration of the cells on the unaffected side, unless there had been disease in childhood of which no history was obtained.

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Case X.—A youth, aged 19, gave a history of two years' ear trouble, during which time he had developed three mastoid abscesses, which had been dealt with by incision only. On admission a retro-auricular fistula was found, and the radiograph shows that the cells are completely obliterated on the affected side. At the operation the antrum and cells were full of pus.

Case XII.—A man, aged 49 (whom you have had the opportunity of examining in the out-patient department to-day), who had suffered from otorrhœa for several years, developed vertigo and vomiting, which came on intermittently during the last five months. There was slight facial paralysis. Radiographically there was little difference between the two sides. The cells were most indistinct and hardly visible, and the shadow of the mastoid suggested that the bone was sclerosed on both sides. At the operation there was no pus in the antrum, but a labyrinthine fistula was present. If we had examined the plate of one side only in this case we would certainly have expected to find pus in the mastoid cells, but with the plate of the other side for comparison we were more than sceptical as to the interpretation of the first plate, especially when we observed that the mastoid itself appeared to be more dense than usual.

Case XIII.—A girl, aged 26, stated that, twelve months previously, she had noted a discharge from her right ear, and shortly afterwards began to suffer from earache. Vertigo was present, and nystagmus to the left side developed in seven seconds. The radiographs show that, on the right, there appears to be sclerosis of the mastoid with almost complete obliteration of the cells, while on the left the mastoid appears to be of normal density although the cells are not so sharply defined as usual. The operation showed that there was a labyrinthine fistula through the fenestra ovalis. There was no actual suppuration in the mastoid at the time of the operation, but the mucous membrane was thickened.

An important question arises from a consideration of these two cases (XII and XIII). Does osteo-sclerosis of the mastoid area conduce to the development of labyrinthine fistulae?

Case XI.—We have purposely placed this case last as it is one that seemed entirely to contradict such evidence as we had obtained as to the value of the X-ray method of examining these cases. The patient was a man, aged 57, who gave a nine months' history of left-sided otorrhœa. For five weeks there had been facial paralysis, while he had recently had to give up work as a painter because of vertigo. Nystagmus was present. The X-ray plates show the cells of the mastoid process most perfectly on both sides, and yet at the operation there was pus in the antrum and mastoid cells. It seemed that there must have been a mistake somewhere, and on looking up the dates we found that the plate of the unaffected side was taken on the day of the operation—you will see the safety-pin in the bandages which were holding the compress in place—and our assistant hurriedly radiographed only one side (the unaffected side!) while we were waiting to operate on the patient. The radiograph of

the affected side—the left—is dated two days later, and we had this plate taken for the sake of completeness and had entirely forgotten the circumstance. This plate therefore shows a mastoid process after the operation, and the clear picture of the cells indicates the perfect drainage which has been secured. On examining the plate of the left side you will be able to detect the area of bone that has been chiselled out, the rounded gougings giving an appearance that almost exactly simulates the appearance of the cells themselves.

This last case has been a stumbling block in the compilation of this paper, for in every single case, apart from this one, we found changes in the mastoid process whenever there was suppuration present in the cells; and now that this case is cleared up we have little hesitation in saying that where radiographs show the mastoid cells equally clearly on the two sides there is no suppuration present within the cells, and this is information of great value if it can be obtained. We say "if" advisedly, for several reasons. The first of these is the technical difficulty of the radiographer in producing exactly similar plates; the X-ray tube is a very fickle instrument, and any alteration of the vacuum within the tube will produce an alteration in the penetrative quality of the rays, resulting in a difference in the negatives of the two sides even though all the other factors have remained constant. Again, if there is an abscess over the mastoid the shadow of the cell outlines will be rendered less distinct, and this must be taken into account in reading the negatives. The degree of haziness due to this cause will vary according to the quantity of pus and also with the penetrative qualities of the X-ray tube where the plate was taken. Then there is the difficulty of immobilizing the head, especially in radiographing the affected side, and when the patient moves another plate has to be taken. The difficulty of reproducing the exact conditions of the first plates is so great that we now think it advisable to take plates of both sides again. The more we see of these cases the more impressed we are by the necessity for the most careful radiography, carried out with such scrupulous attention to detail as is difficult to obtain in the rush of hospital work.

We now turn to the indefinite cases in which the cells are discernible, but hazy. As you will have observed in the cases, this condition is, as expected, usually associated with thickening of the mucous membrane without the presence of actual pus, but we must again insist on the importance of examining two exactly similar plates. Haziness on both sides may be met with, and in this case we would draw no inference either for or against the presence of pus within the cells. It is in these

cases that the most careful comparison of the two sides, and an estimate of the variations due to the technique, are most essential.

In those cases in which no mastoid cells are seen this is due to one of two causes: either the air spaces are obliterated or the radiographs have been taken with a tube of insufficient penetrating power, a fault which an expert radiologist should be able to tell from the general character of the plate by comparing the relative densities of the shadows of the other bones with that cast by the mastoid. It is a matter of experience in the interpretation of radiographs and cannot be readily described. Here is a radiograph of a rachitic tibia. You will note the irregular epiphysial line and other stigmata of rickets, and on the original plate one can see that the bone is so deficient in lime salts, so lacking in density, that its shadow is only slightly deeper than that of the flesh; the lack of density is so marked that the bone would throw only a very faint shadow if the radiograph had been taken with "hard" X-rays. The bone structure shows up quite distinctly, because the rays employed were "soft"—i.e., of little penetrating power—and would reveal slight differences in density. Here is an ordinary radiograph showing a fracture of the head of the radius, and although this was taken with a harder tube yet you will see the outlines and structure of the bones perfectly defined, whereas no bone structure would have been detected if a "soft" tube had been employed, because the rays would not have penetrated the bone at all. Similarly, in these mastoid cases we must use rays that are sufficiently penetrating to pass through all the dense structures, and if we can tell from the shadows of the other bones that the character of the rays is such that the mastoid should throw a shadow of a certain density, and yet the rays have almost entirely failed to penetrate this bone, we are justified in saying that there is a sclerosis of the mastoid process—not a sclerosis of the cortex but a general sclerosis that extends throughout the substance of the bone. In quite a number of the cases we have convinced ourselves of the presence of a sclerosis of this nature, and it is chiefly in those where the disease is of long standing. This observation may be of importance in indicating the direction in which the spread of infection is likely to occur—i.e., towards the labyrinth rather than towards the mastoid. Both apart from, and in conjunction with, the sclerosis we see obliteration of the mastoid cells, and this we believe to be always of pathological significance, but it does not invariably indicate the presence of pus, for old-standing mastoid disease seems to give the same radiographic results in a certain number of cases.

We are fully aware that our experience is as yet comparatively limited and that our conclusions are by no means final. We believe that the method of investigation is likely to prove of great assistance in excluding the presence of pus within the mastoid cells, especially in recent cases, but of less certain value in detecting its presence.

DISCUSSION.

The PRESIDENT (Dr. W. Milligan) said that Dr. Barclay and he had been much interested for some time past in the practicability of applying radiography to the detection of mastoid disease, and he would be glad to hear the experiences of other aural surgeons of this method in this class of disease. Another point of value was the disputed question of sclerosis of the pars mastoidea; what it was, or in fact whether it existed. There was the further point as to whether a mastoid which was dense had anything to do with the production of labyrinthine fistulæ in the external canal, which certainly very commonly occurred. Quite a dozen such cases had been exhibited that morning.

Mr. A. CHEATLE desired to say broadly that the value of radiography in the future would consist not so much in the detection of disease as in the determination of the type of bone present and in the amount of cell distribution. It was unnecessary for him to describe on the present occasion what he called the diploëtic infantile type of bone, and the influence of that type in producing chronic suppuration, but it had a distinct bearing on the subject under discussion. For instance, if the acute middle-ear discharge which occurs in scarlet fever, measles, and other acute infectious diseases did not clear up in a reasonable time and the diploëtic type was determined by radiography, then it would mean that the antrum should be opened through its dense outer wall in order to save the patient from chronic discharge and its complications. He would only bore the meeting if he were to enter into the subject of chronic suppuration, but there was no doubt that this type was responsible in a large measure for chronic suppuration, and indirectly for labyrinthine infection. One anatomical point which had not been worked at, as far as he knew, was the symmetry of the bone in health. He would be reading a paper on the subject at the International Otolological Congress in Boston. He had examined both bones in 120 persons, and found that 82 were symmetrical and 38 asymmetrical; in many the asymmetry was slight, but in some it was very gross. He found that the diploëtic type with a dense outer antral wall was present in normal bones in 24 on both sides and in 20 on one side only, out of the 120. A recital of these figures would explain some of the anomalous results which Dr. Barclay and Dr. Milligan had obtained by means of radiography. One could never depend on the radiograph alone for showing whether

disease existed or not, on account of normal asymmetry. With regard to osteo-sclerosis, he did not think it did not occur, but it was only very local and easily distinguished from the normal dense bone.

Mr. SYDNEY SCOTT said he felt a personal interest in this subject because when Dr. Birkett, of Montreal, brought over some radiograms to the meeting of the British Medical Association in London two years ago, he asked Dr. Birkett his experience of stereoscopic radiograms of the mastoid region, for he felt sure that the stereoscopic methods would prove of interest academically and of importance clinically. Dr. Birkett said he had not tried the stereoscopic methods, but would certainly do so. Mr. Scott asked Dr. Milligan and Dr. Barclay what their experience had been. Personally, he discarded flat radiograms some years ago because he was not convinced that they afforded any more assistance than other methods of clinical examination, but he had found that the introduction of the third dimensional view could be obtained by stereoscopic radiography. He had employed this form of radiography repeatedly during the last two years and now had a series of cases with which he had satisfied himself that the stereoscopic radiograms were of the greatest practical value.

Dr. LOGAN TURNER said that if, when taking the radiograms, the patient's auricle was held forward, a better view would be obtained of the mastoid region. He was investigating the mastoid region by radiography in conjunction with Dr. Porter, of Edinburgh, and their practice was to hold forward the auricle against the plate while the picture was being taken. In some of the radiograms shown that morning the auricle made a shadow which rendered the details less clear. We had to study this subject from the anatomical as well as from the clinical side, and he could not agree with Mr. Cheatle that radiography would be found of no value clinically. The question of mastoid symmetry was one of great importance. Beck, of Chicago, had stated that after radiographing over 300 heads he had found the two mastoid regions symmetrical with one exception. The whole secret of its value depended on whether symmetry existed or not. In the anatomy of the face, it was true that great asymmetry was the rule, and therefore it would be strange if there were a different state of things in the mastoid bones. That, however, was a matter that must be decided. He contended that one did find the radiograph of value in disease. As an illustration he brought for inspection photographs which were taken by Dr. Porter. One was that of a boy who had had acute middle-ear suppuration. Paracentesis had been done, and the patient was not seen again for five or six months. He then returned complaining of pain over the mastoid region. A photograph of both sides was taken, but as they were not good they were discarded, and the boy was kept under observation. His temperature rose at night, and there was tenderness on pressure over the mastoid. He developed œdema over the mastoid, and had a leucocytosis of 14,600. A second radiogram was taken the day before the operation, but it was, unfortunately, not developed until after the operation. The surgeon

opened the mastoid because of the tenderness, the temperature, the oedema, and the leucocytosis. The mastoid was perfectly healthy, and it would be agreed on examining the radiograms that there were healthy-looking cells on the two sides. He put the question whether, if the negative had been developed before the operation, the surgeon would have had the courage to hold his hand, or whether he would have gone on with the operation? Again, there were doubtful cases of what might be termed latent mastoiditis, where there had never been perforation, or if there had been, the tympanic evidence of disease had passed off, and there was normal hearing, no inflammation of the drum-head, but mastoid tenderness and pain. Might not cases of this kind be assisted by the use of the radiogram? He contended that it did help us clinically. Leidler had written a paper on the value of the radiogram in the detection of malignant disease of the ear.¹ Two cases were reported in which the author showed by radiogram that in one of them the malignant disease had spread from the mastoid region to the posterior fossa and into the middle fossa of the skull, and on that evidence he determined it would not be advisable to operate. Use might also be found for radiography in cases of congenital malformation, where we could tell whether we were dealing with a labyrinth, whether the labyrinth was absent, or whether the malformation was limited to the tympanic portion, or involved both the tympanic and the labyrinthine portions of the ear. (Dr. Logan Turner exhibited radiograms.)

Mr. RICHARD LAKE tendered his thanks to the authors, especially as he had not seen the method in actual practice. It was difficult to get good radiograms unless one had a skilled radiographer, and some of the smaller hospitals did not possess such a luxury. He proposed to try and make use of the method.

Mr. E. M. STOCKDALE remarked that he believed radiograms were likely to fall into two classes. In the chronic middle-ear case one might conclude that the mastoid was hard and that the antrum was small and had a firm wall. That would give one kind of shadow. If the antrum communicated with pneumatic or marrow cells, mastoiditis was likely to occur early and give rise to obvious external signs.

Dr. H. J. DAVIS said that one could get a rapid idea of the type of bone present by means of a small transilluminating electric lamp, such as he saw being used in Berlin. The lamp was put inside the meatus, and gave a very brilliant light, and illuminated the mastoid region. If the bone was dense shadows were more opaque than if the bone was cancellous. In a case of mastoiditis the difference on the two sides was very marked. The lamp was in the nature of a minute Heryng's transilluminator, and the principles of illumination were the same.

Dr. BARCLAY, replying on the radiographic points raised, said the stereoscopic method was excellent, but he regretted to say he personally had very poor stereoscopic vision, so he could not appreciate such pictures. But there

¹*Arch. f. Ohrenheilk., Leipz., 1911, lxxxv, pp. 10-20.*

was a difficulty in producing stereoscopic pictures; it was even difficult to get a single plate of a mastoid when it was diseased, as the patients were generally so dull and stupid that they would not keep still. With regard to holding the auricle forward for the purposes of the radiogram, as advocated by Dr. Logan Turner, he had tried it in one case but was not satisfied with it, because the auricle being held forward increased the distance between the plate and the head; also, the holding of the auricle seemed to encourage movement on the part of the patient. Moreover, the shadow cast by the auricle was easily recognized. The electric lamp in the ear seemed to be a simpler method of investigation, except that it did not show the cells themselves.

Dr. MILLIGAN replied on the clinical points raised. He considered that this method of examination was yet only in its infancy. It was difficult to draw any very precise deductions from what had been done so far, but he looked forward to its being of ever-increasing value in the diagnosis of doubtful cases. It must be admitted that there were cases in which it was a delicate point to say whether an operation should or should not be done. That applied more to private than to hospital patients, for in the latter the patients were under one's daily observation and control, and exploratory operation could be carried out without misgiving. But there was a class of private patient in whom it was very desirable to fortify the clinical diagnosis, so far as that could be done, before making use of the knife. If radiography could give any reliable indications in those cases it would be of great value, especially in the early detection of tubercle of the bone. In children one could at times see a deposit on the plate at a spot where it turned out there was tubercle deep in the petrous portion. Dr. Logan Turner referred to the value of radiography in the detection of early malignant disease. There was another class of case. One of the radiograms exhibited that morning, that of a child, showed how beautifully the labyrinth was seen. In practice one was faced with the difficulty of giving advice in certain cases of severe deafness in children, in atresia of the meatus, and in congenital malformation, as to whether anything should be done or not. In that class of case one could see whether there was a labyrinth or not, and he drew attention to the radiograms exhibited downstairs by Dr. Barclay. He did not for a moment deny the infantile type of temporal bone, but it had been doubted whether there was a sclerosis of the mastoid cells themselves. Dr. Barclay and he considered as a result of inspection of the radiograms and in the light of the operative findings, that there was such a condition as sclerosis of the mastoid bone. They did not attempt definitely to rely on the X-ray examination, but, as Dr. Barclay wisely pointed out, they exhausted every possible means of diagnosis first, and then, if there was even a slight element of doubt, X-rays were used. In many of the cases shown that morning there was no doubt about the diagnosis, but the patients were radiographed to see if any further deductions could be obtained from the method and to confirm the clinical examination.

**Demonstration of a Method of studying Degeneration in
Nerve-fibres by means of the Hot Stage.**

By J. LORRAIN SMITH, M.D., and W. MAIR, M.D.

DR. W. MAIR said: Here is a small flat glass bulb, polished on both surfaces. It has set into it two coils of platinum wire and it is filled with liquid paraffin. At one end of it a tube is drawn up, into which a thermometer is inserted. An electric current of the proper strength is sent through the platinum wires, and the whole glass bulb is in consequence heated. This is arranged on the stage of a polarizing microscope. One can lay a microscopic preparation on the hot surface of the glass bulb, and the light comes through the whole. One watches, as the temperature is raised, the point at which the crystals melt. The temperature is controlled by a resistance, by means of which one can set the stage at any required temperature, and the range is from room temperature to over 200° C. Illumination is by the Nernst lamp. It has long been known that the medullated nerve sheath is doubly refracting. On placing a section of spinal cord or medullated nerve under a polarizing microscope, the nerve-fibres are brought out as bright rings. On examining such sections on the hot stage we found that in the normal adult spinal cord this myelin substance has a very extraordinary range of fluid crystalline phase. You can heat it up to 150° C. before the double refraction disappears. On cooling down from that temperature the double refraction reappears. So it appeared to be of interest to examine sections from different pathological conditions to see whether we could detect any difference in the clearing point, because any such differences would indicate chemical changes. The sections were cut with the freezing microtome from formalin-fixed material. We found remarkable differences in the myelin under different conditions. Firstly, with regard to age. A section of spinal cord taken from an infant of a few months old shows a very much lower clearing point than that from an adult. The myelin sheath in the nerve-fibres of the child will clear about 90° to 100° C., whereas an adult goes as high as 150° C. We determined the same thing with normal sections taken from puppies and adult dogs, and there is here also the marked difference due to age. Next we took up the question of secondary degenerations. In a case of fracture of the spine which had gone

sufficiently long to produce considerable degeneration, when one put a section of the cord under the microscope and heated it, the degenerated areas cleared at a very much lower point than did the normal areas. When you get to a particular temperature the degenerated areas appear dark, while the normal areas remain bright. We next wished to investigate conditions in which primary degeneration of the nerve-fibres is known to exist; and we examined sections from cases of general paralysis of the insane. In them we found a marked difference in the clearing point, not of the order which I have mentioned in the case of the child, but a difference of 10° or 20° C. We also found a lower clearing point in cases of pernicious anæmia. This indicated that there is a marked chemical change in these lipoid substances in the central nervous system both in disease and during the course of development; and this led us to approach the question from a purely chemical point of view, and we have been working for some years at the chemical analysis of the lipid substances in the central nervous system. We find that there are distinct chemical differences, corresponding more or less to the differences in clearing point determined on the sections. The most remarkable fact about it is that the complicated lipid bodies known as cerebrosides, which are fatty bodies containing nitrogen but no phosphorus, and which contain sugar, show marked changes. In the child they are present in small quantity only. Gradually, as age increases, these complex cerebrosides are built up and appear in larger quantity in the myelin substance, until the adult stage is reached. In disease they tend to disappear again. In cases of general paralysis of the insane the percentage of cerebroside in the chloroform extract of the dried brain is about half that of the normal brain. There is also a diminution in phosphorus. In degenerated areas in hemiplegia the cerebroside falls off in quantity, there is an increase in cholesterol, and a diminution in phosphorus. It is remarkable how many fatty bodies in the brain show the peculiar physical condition known as the fluid crystalline phase. This stage gives us an excellent means of determining whether a crystalline body has a fluid phase, and if so through what range it extends. The cerebroside has a fluid crystalline phase which extends from body temperature to 200° C. You can heat pure cerebroside on this stage to 200° C. before the double refraction disappears; it is fluid at temperatures much below that. The other important lipid is phosphatide or lecithin, and that shows the same thing—a prolonged phase during which it is in the fluid crystalline condition. These experiments with the pure substances explain why it is that the section

of medullated fibre shows double refraction, and why there is such a range of fluid crystalline phase. We have reason to believe that this method of study will enable us to detect primary degeneration in nerve-fibres at an earlier stage than any staining method, but in the meantime the complexity and interest of the chemical investigation has been such as to allow little opportunity for further microscopical work.

The Cerebrospinal Fluid as an Aid to Diagnosis in Suppurative Meningitis of Otitic Origin.

By F. G. WRIGLEY, M.B.

YOU will all, I am sure, admit that there is often a great difficulty in the diagnosis of suppurative meningitis. The disease often does not follow the typical course described in the text-books, many symptoms which are there regarded as essential being absent. The reason why an accurate diagnosis is often so difficult to make is due to the fact that many of the symptoms of meningitis are present in the other complications of otitis media—e.g., vomiting and optic neuritis are common in brain abscesses, high temperature and rapid pulse in lateral sinus thrombosis. Head retraction frequently occurs in cerebellar abscess; moreover, all the symptoms of suppurative meningitis, though less intense in character, may occur in the condition known as serous meningitis. The importance of an accurate diagnosis is at present chiefly regarded from a prognostic standpoint, for if the suppurative condition can be excluded the prognosis is of course much better.

The examination of the cerebrospinal fluid is of great assistance in determining the presence or absence of this disease if thoroughly carried out, but a cursory examination is often misleading. Before discussing the pathological conditions of the cerebrospinal fluid I will briefly outline its normal condition:—

Tension: The fluid issues drop by drop from the trocar, one drop per second being the normal rate of flow; the normal pressure is 20 to 30 mm. of Hg.

Appearance is clear and watery, free from blood or other colouring matter. The specific gravity varies between 1005 and 1008.

Reaction is alkaline, both in normal and pathological conditions.

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Composition: Water, 99 per cent.; solids, 1 per cent.—NaCl, carbonates, bicarbonates, phosphates, urea, dextrose, and traces of albumin, fat and cholesterin. Dextrose is present normally from 0.2 per cent. to 0.25 per cent. Albumin is only present in slight amount, just enough to give a faint haze on boiling the fluid.

Histology: A few lymphocytes are usually seen in microscopic preparations, often in stages of disintegration.

Bacteriology: The fluid is quite sterile.

THE CONDITION IN SUPPURATIVE MENINGITIS.

In most cases of suppurative meningitis the tension is raised, the fluid often issuing as a continuous stream, and may even spurt to some distance away from the needle. In some cases, however, the tension is lowered; this is uncommon, but does occur when a thick basal exudate prevents free communication between the subarachnoid space at the base of the brain with that of the spinal cord.

Appearance: This is often taken as the index of the presence or absence of suppurative meningitis—if the fluid is clear meningitis is said to be absent, if turbid then present. This is true in the majority of cases, but I have met with three cases which seem to show that this is not always an infallible test.

In two cases of brain abscess in which the cerebrospinal fluid was quite turbid there was increased albumin (0.18 per cent. Esbach in one case and 0.2 per cent. Esbach in the other), the tension was markedly raised, and a marked polymorphonuclear leucocytosis was present in films made from the fluid. One was a temporo-sphenoidal abscess, which was drained by operation: the case ended fatally and at the post-mortem there was a large abscess cavity, the rest of the temporal lobe being infiltrated with pus and somewhat resembling a cellulitis. There was a slight injection of the basal meninges but no definite meningitis. The other case was a cerebellar abscess: a radical mastoid operation had been done ten days before; meningitis was diagnosed and a decompression operation decided upon. A trephine opening was made over the cerebellum as a start, but, as the brain was not pulsating, the cerebellum was explored and an abscess containing $\frac{1}{2}$ oz. of pus was found and drained. Nothing further was done and the patient made a complete recovery. In each of these cases the condition of the cerebrospinal fluid was the same, the important point being that no bacteria were found in either case either in microscopic films or in cultures, eight

punctures being made in the first case and three in the second. Another point of resemblance is that each case was apparently an acute form of abscess: in the fatal one there was no sign of the formation of a capsule round the abscess, and in the second case no capsule was at the time noticed round the abscess and no resistance was felt when the substance of the cerebellum was explored. From these two cases it would appear that a turbid cerebrospinal fluid is not of itself sufficient evidence for the diagnosis of suppurative meningitis.

The third case was a temporo-sphenoidal abscess. The cerebrospinal fluid was under high tension and quite clear in appearance. On standing for an hour or so a well-marked coagulum was deposited, histological examination of which revealed a large number of polynuclear leucocytes and numerous clumps of staphylococci. The patient died and post mortem there was a well-marked basal meningitis. A lumbar puncture done the day before death gave similar results to the first one. This case seems to show that suppurative meningitis may be present with a clear cerebrospinal fluid which may contain bacteria, and that a clear cerebrospinal fluid is not sufficient by itself to exclude suppurative meningitis.

The question of the exclusion of meningitis seems to turn on the histological and bacteriological examination of the fluid, and I do not think that any examination which does not include these should be used as conclusive evidence one way or the other. If the nature of the fluid suggests suppurative meningitis and bacteria are not found by the microscope, then, before making an absolute diagnosis, cultures should be made. In practice this, of course, would be difficult, as cases are often too urgent for time to be lost in having the cultures prepared. In these cases I would suggest that if bacteria are not found in the cerebrospinal fluid by the microscope and any operation is undertaken, it should include exploration of the cerebellum and temporo-sphenoidal lobe. Even if meningitis is present little or no harm would be done, and it might be the means of bringing to light an abscess of which no definite symptoms were present.

Another feature which may be of use is the estimation of the amount of glucose present. It has been stated that the amount of glucose present in the cerebrospinal fluid diminishes in meningitis, disappearing as the disease progresses. I have estimated the sugar in eleven cases (twelve punctures) and found it normal in eight specimens; in the other four the results were:—

Case I.—First puncture, 0.14 per cent.; second puncture, 0.08 per cent.

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Case II.—There was no reduction with Fehling's solution.

Case III.—No reduction with Fehling's solution.

From this it would seem that the amount of sugar may diminish in suppurative meningitis, and that although the fact may not be of the first importance the absence or diminution of the amount might be taken into account as an additional confirmation of the existence of meningitis. Albumin is increased in suppurative meningitis; this is easily seen on boiling a tube, when the faint haze of the normal fluid is replaced by a definite opacity. In all cases in which I have estimated the amount of albumin it has been 0.1 per cent. or above.

Histology: There is generally an increased leucocytosis in the cerebrospinal fluid in meningitis. Two leucocytes to a field is said to be the normal. The leucocytosis chiefly affects the polynuclear leucocytes, though the lymphocytes are also increased.

Bacteriology: The organisms most commonly found in the cerebrospinal fluid are the same as those found in the ear: A Gram-negative diplococcus (? *Diplococcus catarrhalis*), streptococci, staphylococci; also found, though more rarely, are, *Bacillus coli communis*, *Bacillus proteus vulgaris*, Friedländer's bacillus.

The diagnosis of suppurative meningitis cannot be made with certainty (though it may exist) without the presence of bacteria in the cerebrospinal fluid, and I consider that the following features are usually necessary before an absolute diagnosis can be made: The fluid is either turbid or deposits a coagulum quickly on standing. The albumin is increased 0.1 per cent. Esbach or above. Microscopic examination shows a polymorphonuclear leucocytosis, and bacteria are found either in films or cultures. If these features are present the diagnosis may be made with certainty.

I am indebted to Dr. Milligan for permission to use the three illustrative cases.

DISCUSSION.

Mr. C. A. BALLANCE said that in recent years they had all been interested in meningitis, and he agreed that the condition could not be diagnosed by the clinical symptoms alone. The only definite evidence that meningitis was present was the discovery of the causal organism in cerebrospinal fluid. With regard to treatment, he was very much interested, when in Copenhagen last autumn, in seeing Dr. Mygind's cases. Dr. Mygind had written papers on the treatment of meningitis, and he had a number of cases brought up for

his inspection. They were almost all aural cases, and Dr. Mygind considered that the cases of meningitis which came on after operation on the temporal bone were almost always fatal. Some of the cases in which the onset antedated the operation could be saved. The operations which Dr. Mygind looked upon as most important were, first the removal of the source of infection; all would agree with this. Dr. Mygind had also planned a definite operation in the shape of a decompression—i.e., he removed the bone over a definite area, $1\frac{1}{2}$ to 2 sq. in. in the region of the original site of infection—and he sometimes opened the dura. He (Mr. Ballance) was surprised to find that in some cases which recovered the dura had not been opened, but there had been only removal of a portion of the bone, which he did not regard as a decompression operation at all. This term should include incision of the dura. In all the cases which Dr. Mygind had treated he did not recognize the presence of meningitis unless there was turbid cerebrospinal fluid and he could grow an organism from it. This was a most important and valuable point, because it limited one to definite evidence of pyogenic inflammation of the meninges. Otherwise one might be reporting cases as meningitis which were not so, and some wonderful operation might be carried out on them and cure attributed to it which might have occurred in any case. With regard to the operations which he (Mr. Ballance) did, he had made large craniectomies in the occipital region and endeavoured to drain the large cisternæ at the base of the brain, but he had been struck by the fact that the more complete, apparently, the operation was the more likely was the patient to die. For this reason he was much interested in the decompression operations which Dr. Mygind did, for he in all cases combined decompression with lumbar puncture; and what one had generally to do in cases of general meningitis—he did not include the fulminating cases which killed the patient in thirty-six or forty-eight hours, but those which lasted a week and in which in future could perhaps be arrested—was, first of all removal of the primary disease, which was absolutely essential, and subsequently a small local craniectomy with incision of the dura, but always lumbar puncture repeated day by day. He thought it absolutely essential, so as to arrest the meningitis, that one should get rid of the intradural pressure. If one did so, for some reason certain pathogenic micro-organisms were not able to grow as they grew under conditions of pressure. And if that pressure were relieved, as Mygind had done in some of his cases, or if one did lumbar puncture, or combined these methods, then in a certain proportion of these cases one would be able to arrest the progress of what was believed to be general meningitis. In addition it was of the first importance to use a vaccine as soon as possible. An autogenous vaccine required some time for its manufacture, but when the particular micro-organism was known, one could use a stock vaccine, or a stock antitoxic serum.

Dr. THOMAS BARR said that a very important point in regard to this subject was the distinction between serous meningitis and purulent meningitis. It was generally held that if polymorphonuclear cells and pathogenic organisms were found in the cerebrospinal fluid derived from lumbar puncture the case

was necessarily one of purulent meningitis. But some time ago he saw a case which showed the incorrectness of this view. The case was that of a young man under the charge of Dr. Stoddart Barr and presented typical symptoms of meningitis in connexion with otorrhœa of four years' duration. The radical mastoid operation was performed by Dr. Stoddart Barr, and the lateral sinus was exposed and granulation tissue with purulent matter was found on its outer surface. After a few days, during which the meningeal symptoms continued with extraordinarily severe pain in the head, a remarkable bulging was observed in the neighbourhood of the sinus. At first it was thought that the sinus had become the seat of a thrombus, but the swelling was large and elastic, and it was decided that it was due to a bulging of the dura mater by fluid underneath. In the absence of Dr. Barr, Dr. Syme did lumbar puncture, and fluid escaped under very considerable pressure. The immediate result was the disappearance of the headache, which did not return, while the bulging referred to quickly diminished and in a short time disappeared. The pathologist's report was to the effect that the fluid was slightly turbid, that it contained abundant polymorphonuclear cells and a Gram-negative diplococcus. This report pointed, apparently, to purulent meningitis, but the result showed that it was probably serous meningitis, and there was an uninterrupted recovery. The young man was now perfectly well.

Dr. A. BRONNER remarked that in cerebral tumour with increased pressure, when lumbar puncture was done and there was little or no fluid, this was said to be due to occlusion of the foramen magnum due to pressure. If it were due to inflammation one would often find similar conditions in meningitis.

Mr. WEST said that with regard to examination of cerebrospinal fluid as an aid to diagnosis, he thought all could agree with almost everything which Mr. Wrigley said. It had been emphasized by the pertinent experience of members that the mere fact of turbid fluid existing did not help one in the diagnosis of meningitis unless investigation were carried further. In a recent discussion held before the Society on brain abscess, he drew attention to the fact that in cerebellar abscess it was characteristic to get not only many other symptoms of meningitis, such as head retraction, but to get cloudy cerebrospinal fluid.¹ The fluid was very rich in polymorphonuclear leucocytes, but was sterile. With regard to the treatment of meningitis, he had very little to say which was new, but one naturally looked at the matter from the standpoint of personal experience. It was always possible to prevent pressure being the cause of death in meningitis; and without a decompression operation—i.e., with only lumbar puncture. Lumbar drainage by retention of the cannula, or translabyrinthine drainage through the meatus, would give the same result, and perhaps even more efficiently. But his experience was that although one could in this way deal with many of the most distressing symptoms of meningitis, in most of those cases death would occur. He had

¹ *Proceedings*, p. 72.

seen only three patients recover from proved meningitis. Death occurred from the steady progress of the infection in the meninges. So, finally, one would find a patient whose meningeal surface was almost dry, and yet there was a thick layer of inflammatory material spread all over the base, and creeping up along the fissure of Sylvius, and that patient died of general sepsis or of disintegration of brain from local sepsis. One wished to prolong the patient's life by drainage, so that death did not occur from pressure, and also by doing all possible to increase the resistive power. His experience of vaccines in these cases had been totally disappointing. He asked whether members present had investigated the question in the way of trying "sensitized" vaccines. He understood that they could be given in almost unlimited quantity, and without producing what was known as the negative phase. In that way we might get a step further in the treatment of meningitis.

Mr. CHARLES G. LEE said he understood it had been stated that repeated drainage would result in lowered pressure. He wondered whether the Section was acquainted with the work of Dr. Alexander on epilepsy. Dr. Alexander, with the idea of permanently reducing pressure and stopping the fits, had been removing the parietal bone, then cutting strips of the dura out, leaving strips intact. He claimed to have brought about in this way what he desired. Possibly this course would be better than the repeated lumbar punctures which had been advocated at this meeting, and which Mr. Lee believed were not always unattended with serious consequences.

Mr. SYDNEY SCOTT said that until five years or more ago it was considered that meningitis should be classed among the invariably fatal complications of ear disease. Early diagnosis and prompt intervention seemed to alter this view. The question now arose as to what constituted meningitis. Personally, he only accepted meningitis for the diagnosis when the cerebrospinal fluid contained bacteria. A second question had arisen—what class of case had a chance of recovery? The time was too short to go fully into these points at this meeting, but he would like to relate some of the chief features bearing on the subject which occurred in the case of a patient whom he had been called to see on account of violent headache following hemorrhagic otitis media (unilateral). The hemorrhage had been quite slight, but a small clot still obscured the landmarks of the tympanic membrane. The deafness was not great, the whisper and watch being audible on the affected side. The fork was lateralized from the forehead to the same side. The headache was the chief symptom. He found the patient had vomited six times during the morning. He described the pain as resembling that of a tight band around the head. The pupils were fixed, and the tendon reflexes were abolished. There was a marked white *tache cérébrale*. He had only seen a white tache in one other case (pneumococcal meningitis, fatal). He was afraid lest this patient was already doomed; however, he operated almost at once, that is, in about three hours, and, contrary to his expectation, found that the whole of the mastoid process was of the pneumatic (coarsely cellular) variety, and that the cells

were absolutely normal air-containing cells without any sign of inflammation. Nevertheless the antrum, which was exposed on account of the tympanic appearances, was found to contain blood-stained fluid, which was found to be swarming with pyogenic streptococci (Gordon tests by Dr. Pritchard). The dura mater was exposed and was obviously hyperæmic; it was not incised or punctured. The antrum was drained by tube and the incision closed around it by suture in the usual method of performing Schwartz's operation. The lumbar puncture yielded cloudy cerebrospinal fluid, which escaped under pressure. The albuminous content was increased, polymorphous nuclear cells were abundant, and streptococci were discovered in films and grew in long chains on culture, conforming to pyogenes in the sugar tests (Dr. Pritchard). The result of the operation was an arrest of the symptoms. A second puncture two days later yielded normal cerebrospinal fluid under normal tension, free from excess of cells and of bacteria. Normal saline was given at first *per rectum*, before and after the operation; on the second and third days after operation the saline was given intravenously. The patient gradually improved after passing through a critical stage of wild delirium, and he left the nursing home in the third week with the wound healed and apparently quite recovered. A second case of meningitis which recovered was admitted with sixth nerve palsy, and pneumococci were present in the mastoid pus and in the cerebrospinal fluid withdrawn by lumbar puncture. The simple mastoid operation, lumbar puncture, and the introduction of salines, were the only measures adopted. Had vaccines or anti-sera been used in the above cases the recovery would probably have been attributed to these agents, but the omission to employ these remedies in these instances served as evidence that there was a class of meningitis which resolved without any very clear explanation of the reason.

The PRESIDENT (Dr. W. Milligan) said that Mr. Wrigley must feel encouraged by the remarks which had been made about his paper, and they would help him to go on with his investigation. In the Royal Infirmary they never regarded a case as one of purulent meningitis unless bacteria could be found under the microscope or cultivated on films. Cases in which no bacteria could be found were classified as serous meningitis, however turbid the cerebrospinal fluid might be. A fair number of decompression operations had been done in his department, and not only was a piece of bone cut away, but a portion of the dura also. Two cases of cured purulent meningitis of the posterior fossa had been shown that morning in which bacteria were found in the cerebrospinal fluid. In one the organism was the *Diplococcus catarrhalis*, in the other the streptococcus. Recovery occurred in both.

Mr. WRIGLEY, in reply, said that with regard to the question of not getting cerebrospinal fluid in brain tumour, he had seen one case of meningitis in which he got 2 dr. of pus and nothing further; post mortem the brain was found to be very œdematous and there was a thick exudate over the basal meninges. In three other cases of septic meningitis he got no cerebrospinal fluid at all.

Demonstration of Cases.

By W. MILLIGAN, M.D.

(1) MRS. C. Chronic right-sided suppurative otitis media of many years' duration; constant pain over right side of head; mental hebetude. Operation in June, 1897: Abscess in temporo-sphenoidal lobe, containing 3 oz. of pus, opened. Drainage with rubber tube; mixed infection, streptococci and staphylococci being much in evidence.

(2) H. W. Large temporo-sphenoidal abscess, the result of chronic suppurative middle-ear disease, containing 2 oz. of pus, evacuated in 1905. Mixed infection, but mainly streptococcal.

(3) H. P., male, aged 36. Right chronic suppurative otitis media of two years' duration: temporo-sphenoidal abscess. Symptoms: Headache, vomiting, constipation; temperature 102° F., pulse 90 (later, temperature 98° F., pulse 44); no nystagmus, ptosis, or optic neuritis. Cerebrospinal fluid rather cloudy; tension increased; increased albumin and leucocytes, no bacteria. After two days well-marked ptosis was noticed. Operation (April 28, 1910): Post-aural operation; cholesteatoma, large temporo-sphenoidal abscess containing 2 oz. of pus and shreds of brain tissue, counter-drain directly over the lobe. Slight brain hernia developed; reduced by pressure.

(4) A. D., male, aged 24. Right chronic suppurative otitis media of eighteen years' duration; cerebellar abscess. Symptoms: Vomiting, vertigo, occipital headache, constipation; mental condition drowsy; temperature 97° F., pulse, 56. Spontaneous nystagmus towards lesion. Well-marked optic neuritis (right and left); facial paralysis (right). Cerebrospinal fluid clear; tension increased; slight increase of albumin; no bacteria. Operation (February 20, 1910): Post-aural operation, fistula into antrum; extensive cholesteatoma. The cerebellum was explored in front of the lateral sinus, and an abscess containing about 2 oz. of pus was found. Blood count: Leucocytosis, 14,000. The radical mastoid operation was completed a month later.

(5) E. S., aged 16. Suppurative otitis media of many years' duration. Admitted, complaining of occipital headache, sickness, and vertigo. Pulse 54, temperature 96.4° F., respirations 14. Radical mastoid; opening of cerebellum through posterior wall of mastoid; 1½ oz. of pus evacuated; drainage by rubber tube. Return of headache. Decompression operation (posterior fossa): Removal of pus from subdural space; complete recovery.

(6) L. G., female, aged 21. Chronic right suppurative otitis media of many years' duration; middle ear disorganized and full of granulation tissue. Symptoms: Vomiting, vertigo, occipital pain, mental hebetude, staggering gait. Operation: Post-aural operation followed by opening up of cerebellar

abscess through posterior mastoid wall; 2 oz. of pus evacuated; drainage by means of rubber tube.

(7) M. J., male, aged 30. Chronic suppurative otitis media (left) since infancy; extradural abscess (middle fossa); serous meningitis. Symptoms: Headache, vomiting; temperature 100° F. Hearing: Watch not heard at all; tuning forks lateralized to right ear. Caloric tests negative. Optic neuritis left disk. Cerebrospinal fluid: Clear, under high tension; no bacteria. Operation (June 23, 1911): Post-aural operation; cholesteatoma; extradural abscess over middle fossa, sinus running into temporo-sphenoidal lobe, but no abscess in brain. Radical operation completed fourteen days later.

(8) H. W., female, aged 38. Chronic suppurative otitis media (right); serous meningitis. Symptoms: Temperature 100.2° F.; slight head retraction; headache; several attacks of vomiting; congestion of right optic disk. Cerebrospinal fluid: Clear, under high tension; no bacteria. Operation (April 29, 1911): Small cholesteatoma; roof of middle ear carious; temporo-sphenoidal lobe bulged down into wound but no abscess found. A large amount of cerebrospinal fluid drained away from the cisterna pontis; this continued for several days after operation. Symptoms disappeared a week after operation.

(9) F. S., female, aged 19. Right suppurative otitis media of ten years' duration; ? serous meningitis. Symptoms: Occipital headache, vomiting, vertigo, slight mental apathy; temperature 100° F. Complete prolapse of upper and posterior wall, ear discharging freely. Hearing: Watch not heard at all; tuning fork lateralized to the right ear. Caloric tests normal; doubtful fistula nystagmus. Eyes: No spontaneous nystagmus; paralysis of right external rectus; optic neuritis right > left. Cerebrospinal fluid: Slightly turbid; excess of lymphocytes. Operation (April, 1911): Post-aural operation; very extensive cholesteatoma; no dura exposed, and no sign of labyrinthine fistula.

(10) P. B. For five years suffered from constant vertigo and incessant tinnitus, quite unable to work; under medicinal treatment for five years. Operation: Extirpation of vestibulo-canalicular system; complete relief from vertiginous symptoms.

(11) L. J., female, aged 19. Otitis media suppurativa of many years' duration; before admission frequent attacks of vertigo and vomiting; meatus full of granulation tissue, bare bone felt with probe. Watch heard on contact. Caloric tests positive, both hot and cold, syringing bringing on nystagmus in fifteen to twenty seconds. "Fistel-symptom" well marked on compression with air-douche, also on pressing tragus inwards; marked Rombergism; no optic neuritis. Operation: Complete post-aural operation; large fistula found in external canal.

(12) J. F., male, aged 17. Chronic suppurative otitis media (left) of fifteen years' duration; fistula into external canal. Symptoms: Temperature 99.8° F., vertigo, vomiting, pain in left ear. Hearing: Watch not heard at all; tuning

forks lateralized to left ear. Nystagmus: Spontaneous nystagmus towards right side; caloric tests indefinite, no fistula nystagmus; marked Rombergism. Operation (September 21, 1911): Post-aural operation; fistula in bony portion of external canal.

(13) A. L., male, aged 35. Chronic suppurative otitis media (right) of ten years' duration. Symptoms: Dizziness on syringing ear. Hearing: Watch heard 1 in. from ear; tuning forks lateralized to right ear. Nystagmus: Slight spontaneous nystagmus to both sides. Caloric reaction: Positive result obtained in ten seconds; fistula nystagmus well marked; fairly well marked Rombergism. Operation (April 27, 1911): Post-aural operation; small cholesteatoma; large fistula on posterior limb of external canal.

(14) L. B., aged 26. Right-sided suppurative otitis media of twelve months' duration; severe vertigo. Caloric reaction: Nystagmus to opposite side in seven seconds. Radical mastoid operation: Stapes absent; pus from vestibule; opening up and drainage of vestibule. Subsequent treatment by packing. Blood count:—

		Before operation		Two days after		Five days after		Nine days after
Total	...	14,500	...	7,500	...	12,000	...	15,000
Polymorphonuclears	...	69 per cent.	...	80 per cent.	...	80 per cent.	...	78 per cent.
Large lymphocytes	...	14	..	4	..	4	..	8
Small lymphocytes	...	16	..	10	..	10	..	14

Patient started with earache and slight discharge from the left ear.

(15) A. U., female, aged 15. Right-sided suppurative otitis media of many years' duration; right-sided facial paralysis; no nystagmus. Optic neuritis right disk. Hearing power *nil*; tuning forks lateralized to left side; marked Rombergism. Radical mastoid operation and labyrinthectomy; cholesteatoma found invading cochlea.

(16) H. H., male, aged 11. Left otitis media suppurativa of four years' duration. Previous to admission had complained of severe headache, frequent attacks of sickness, and marked vertigo. Watch heard on contact; tuning fork tests lateralized to left side. Caloric tests positive and rapidly obtained. "Fistula nystagmus" well marked; slight spontaneous nystagmus to right side. No optic neuritis. Temperature 99°6' F., pulse 56-96, respirations 20. Radical mastoid operation: Large fistula found in posterior part of external canal; wound left open.

(17) E. T., aged 32. Complete labyrinthectomy for chronic suppurative labyrinthitis eight years ago. Complete freedom from all symptoms.

(18) J. H., male, aged 49. Left suppurative otitis media of many years' duration; severe vertigo for five months. Facial paralysis; fistula nystagmus; well-marked Rombergism. Radical mastoid operation and exposure of outer labyrinthine wall; large fistula found. Facial paralysis much improved since operation; vertigo practically gone.

(19) J. K., male, aged 25. Chronic suppurative otitis media (left) of sixteen years' duration. Symptoms: Headache and dizziness. Hearing: Watch heard 2 in. from ear; tuning forks lateralized to left ear. Caloric tests: Positive result obtained in 15 to 20 seconds; fistula nystagmus well marked, also on pressing tragus inwards; no Rombergism. Operation (March 16, 1911): Post-aural operation: small cholesteatoma; large fistula on external canal; ossicles and membrane left intact.

(20) J. B., male, aged 28. Bezold's mastoiditis; five weeks' earache, discharge; no facial paralysis, no vertigo, no emesis, no nystagmus. Cerebro-spinal fluid normal in colour and pressure; œdema and tenderness over apex of mastoid and in neck. Operation: Perforation of apex of mastoid below and in front; dura mater exposed in post-cranial fossa. Healed up well. Day report—blood counts:—

		Before operation		First day after operation		One week later		Three weeks after operation
Total	...	14,800	...	12,000	...	9,600	...	9,000
Polymorphonuclears	...	65 per cent.	...	65 per cent.	...	75 per cent.	...	53.5 per cent.
Small lymphocytes	...	29	..	30	..	14	..	22.5
Large lymphocytes	...	16	..	15	..	4.5	..	13.5
								3.5
								Eosinophiles

(21) A. A., male, aged 22. Right otitis media suppurativa of four months' duration. Temperature 99°6' F., pulse 103. Free discharge from ear; prolapse of postero-superior meatal wall; tenderness and œdema over apex and down side of neck; on deep pressure pus welled up into ear; slight facial paralysis of three weeks' duration. Operation: Mastoid cortex thick, apical fistula; diseased cells cleared out, drainage-tube passed into neck.

(22) T. F., male, aged 18. Chronic right suppurative otitis media of many years' duration. Extensive cholesteatoma, from middle fossa to apex of mastoid and exposing lateral sinus. Operation (October 6, 1910): Complete post-aural operation.

(23) H. R., male, aged 34. Three weeks' history of suppuration; small perforation in posterior segment of left tympanic membrane; mastoid perioritis and post-auricular abscess. Operation (September 29, 1910): Fistula into antrum; large cholesteatoma extending backwards and exposing area of cerebellum. A complete radical mastoid was performed.

(24) T. L., aged 22. Otitis media suppurativa of several years' duration; pain over mastoid; profuse discharge; cholesteatoma found; lateral sinus exposed at bottom of wound, perisinus abscess. Lateral sinus opened to allow of removal of cholesteatoma surrounding it. Treatment by application of "scarlet red" (4 per cent. solution in olive oil).

(25) M. M., aged 17. Acute mastoiditis; extradural abscess in posterior fossa. Mastoid cells opened; disease traced backwards; posterior fossa opened and large extradural abscess evacuated.

(26) F. M., aged 41. Chronic right suppurative otitis media (twenty-five years' duration); extensive cholesteatoma in posterior fossa reaching as far as internal auditory meatus.

(27) F. W., female, aged 17. Chronic suppurative otitis media (left) of three years' duration; mastoid periostitis. Operation (August 10, 1911): Radical mastoid with preservation of ossicles and membrane; small antrum containing cholesteatoma.

(28) W. A. B., aged 16. Three weeks' history of nasal discharge; fistula through floor of frontal sinus; very extensive orbital cellulitis. Frontal sinus opened up; dura mater of anterior fossa found largely exposed; large drainage tube passed into nose; partial closure of external wound at time of operation.

Demonstration of Cases.

By F. H. WESTMACOTT, F.R.C.S.

(1) *Radical Mastoid*.—Operation, November 21, 1911; healed, April 23, 1912. Posterior wound left open to granulate. Posterior wall of cartilaginous meatus excised.

(2) *Inclusion Cyst in the Meatus after a Radical Mastoid Operation*.—A boy, aged 9. A bluish, non-pulsating polypoid protrusion was present in the opening of the meatus. This came gradually after discharge from an infectious disease hospital, where the operation was done. The cyst burst three weeks ago, and blood-stained fluid came away. The cyst is now filling up again.

(3) *Chronic Hyperplasia of Superior Maxilla*.—Slow enlargement of maxilla, with invasion of Highmore cavity by sponge-like bone. Microscopical examination shows no sign of inflammation or new growth. Described in Dreschfeld Memorial Volume, 1908. Removal of growth, November 3, 1908.

Demonstration of Cases.

By J. ARNOLD JONES, F.R.C.S.Ed.

(1) *Hysterical Deafness*.—Girl, aged 5. First seen in 1910. Had been quite well up to six months previously; she had then run into a lamp-post, and had hurt her nose and "got two black eyes." No loss of consciousness; was not confined to bed; had no further symptoms. Two days after the accident ceased to speak or hear, both of which she had previously been perfectly capable of. No tinnitus or vertigo. On examination: Wax removed from both external auditory meati; drums slightly retracted; adenoids and enlarged

tonsils present. The child took no notice of voice, tuning forks, or loud noises. Four months later adenoids and tonsils removed; no improvement followed. No other hysterical stigmata have been observed.

(2) *Hysterical Deafness*.—Girl, aged 10. Went to bed on November 27, 1910, quite well in every respect; awoke on November 28, stone deaf. First seen December 1, 1910; no tinnitus or vertigo. On examination: Both drums slightly retracted; adenoids present. Examination with tuning forks, voice, &c., proved contradictory—e.g., she denied hearing loudly vibrating forks, but once or twice declared she heard forks which were not vibrating. Bone-conduction apparently much reduced. No history of previous organic disease. Adenoids removed in hospital, January, 1911. Nurses testified that at times she replied to ordinary voice. About this period she had one or two attacks of temporary blindness and aphonia. Has remained deaf to the human voice ever since. Has had inflation, oto-massage, and various drugs.

(3) *Stapes removed with Aural Polyp; Improved Hearing*.—Patient was operated on for removal of an aural polypus on April 11, 1912. Polypus removed by snare in usual manner. After removal the stapes was noticed to be attached to the distal end of the polypus. Recovery entirely uneventful; suppuration cured; hears better than before operation. (Stapes shown in bottle.)

(4) *Radical Mastoid Operation for Cure of Chronic Suppuration; Fistula, External Semicircular Canal*.—On January 7, 1911, patient complained of vertigo of six weeks' duration, and chronic suppuration in the right ear of many years' duration. Pain in right ear. On examination: Pus in external meatus; aural polyp, and bulging of post-suppurative meatal wall; slight mastoid tenderness. Caloric (cold) test produced no response, probably on account of polyp and obstruction in external meatus. Radical mastoid operation performed on February 2, 1911. Much necrosis of bone, especially in neighbourhood of the Fallopian aqueduct; fistula, external semicircular canal; granulations present in fistula. These were gently curetted—usual meatal flap. Uneventful recovery. June 6, 1912: Response to caloric (cold) test in forty seconds.

Demonstration of Cases.

By T. H. PINDER, M.R.C.S.

(1) *Radical Mastoid (Left Ear) and Radical Mastoid and Temporo-sphenoidal Abscess (Right Ear)*.—Symptoms: Pain, headache, vomiting, head retraction; Kernig's sign present; temperature 103° F., pulse 120. After admission, pulse dropped to 72, temperature 97.6° F. Operation (October 12, 1906): Complete post-aural operation; extradural abscess over lateral sinus and large area of cerebellum; temperature 99° F., pulse 75. October 15:

Fainting frequent. October 17: Fainting frequent; temperature 99° F., pulse 55; very drowsy; consciousness impaired; pupils widely dilated. Operation (October 17, 1906): Temporo-sphenoidal lobe exposed; large abscess found containing at least 2 oz. of pus and shreds of necrosed brain tissue; rubber drainage-tube inserted. October 18, 1906: Consciousness returning; no more vomiting. October 22, 1906: Swelling and œdema of right optic disk; difficulty experienced in drainage of abscess—two tubes inserted, one large one just into abscess cavity and a smaller one inside the larger right up to wall of abscess. November 20, 1906: Abscess drying. December 18, 1906: Slight discharge. February 20, 1907: Middle ear and abscess quite dry. The hearing on both sides is at present so good that she plays the mandolin in public as a member of a band.

(2) *Left Chronic Suppurative Otitis Media; Lateral Sinus Thrombosis.*—H. W., aged 21. Suppurative otitis media of fourteen years' duration. Symptoms: Pain, headache, repeated rigors, mental apathy; temperature 104.4° F. Operation (April 10, 1912): Post-aural operation; antrum contained pus under tension and a cholesteatoma which ran backwards and exposed the lateral sinus, and also a large area of the middle fossa. The sinus wall was gangrenous and its lumen was filled with thrombus for 1½ in. of its length. After operation the temperature dropped, but in the course of the next day patient had a slight rigor, which was repeated with greater severity the following day (temperature 105° F.). Operation (April 13, 1912): Ligature of internal jugular. The temperature remained high but no rigors occurred. There was a little effusion at the base of the right lung which cleared up in a few days. The temperature and pulse came down to normal in about ten days.

(3) *Acute Mastoiditis (Right); Lateral Sinus Thrombosis.*—E. W., girl, aged 6. Acute otitis media three weeks before admission. Symptoms: Pain and headache, vomiting and repeated rigors; temperature 100.2° F., pulse 110, respirations 20. Two rigors occurred the day after admission (temperature 104° F.). Operation (August 12, 1910): Antrectomy (antrum appeared normal); circumsinusal abscess found on exposing lateral sinus. The sinus wall appeared normal, but on opening it a clot 1 in. in length was found; it had begun to break down. The thrombus was removed and the internal jugular vein ligatured. High temperature and rigors continued after the operation for two or three weeks. After that time the rigors ceased and the temperature gradually came down to the normal. Ear quite dry and wound healed on discharge from hospital.

(4) *Right Chronic Suppurative Otitis Media of Six Months' Duration; Lateral Sinus Thrombosis.*—Symptoms: Pain, headache, mastoid periostitis, Bezold's mastoiditis; temperature 102.4° F. Operation (July 6, 1906): Incision of mastoid abscess and free incision of cervical abscess. On July 10 patient had a rigor; temperature 104.8° F., pulse 130. Operation (July 11, 1906): Post-aural operation; cholesteatoma; sinus exposed, no perisinus

abscess, and sinus pulsating. On July 12 and 13 rigor again occurred. Marked internal squint. Operation (July 13, 1906): Sinus opened and large clot removed; free hemorrhage from torcular end of sinus; outer wall of sinus excised; slight oozing from jugular end. July 15, 1906: Rigor repeated; temperature 105.2° F. Operation: Ligature of internal jugular. July 16, 1906: Rigors repeated (three times); temperature 106.2° F.; optic neuritis and septic choroiditis. The rigors continued till July 20, after which they were not repeated. The temperature gradually fell to normal. Squint quite recovered from by September 25, 1906.

Demonstration of Cases.

By D. LINDLEY SEWELL, M.B.

(1) *Chronic Suppurative Otitis Media (Left); Lateral Sinus Thrombosis.*—L. T., male, aged 21. Left chronic suppurative otitis media of five or six years' duration. Symptoms: Pain and headache, vomiting, repeated rigors; temperature 100.4° F., pulse 100, respirations 18. Cerebrospinal fluid normal. Patient was admitted about 8.30 p.m., and at 10 p.m. had a rigor; temperature 103.6° F. Operation (October 14, 1911): Post-aural operation; mastoid full of granulation tissue and pus; lateral sinus exposed and appeared to be gangrenous and was surrounded by a perisinus abscess. The lateral sinus was opened and a clot 2 in. in length removed; it did not appear to have broken down. The jugular vein was *not* ligatured. The post-aural wound was closed three weeks after the operation.

(2) *Chronic Left Suppurative Otitis Media; Lateral Sinus Thrombosis.*—W. F., aged 24. Left suppurative otitis media of many years' duration. Symptoms: Pain (headache), repeated rigors, no vomiting; temperature 101.2° F., pulse 100, respirations 20. Hearing: Watch not heard; tuning fork lateralized to left side; caloric tests positive; no fistula symptom. Cerebrospinal fluid: Tension increased, slight increase of albumin, otherwise normal. Rigor occurred on evening of admission (October 27, 1911). Operation (October 28, 1911): Post-aural operation; mastoid contained cholesteatoma; large and very foul collection of pus around lateral sinus. The sinus itself contained a thrombus of 2 in. in length extending towards the jugular bulb. It was decided not to ligature the internal jugular owing to patient's condition, which was bad. There was marked improvement for the first day, but on the day following that patient had two rigors (temperature 103.6° F. and 105° F.). Operation: Ligature of internal jugular; the vein was tied in the neck and traced upwards to the mastoid; it was then washed through from the neck to the sinus by syringing with lotion. No further rigors after second operation.

(3) *Cerebellar Abscess following Chronic Middle-ear Suppuration (Right).*—R. C., male. Right chronic suppurative otitis media of many years'

duration. Symptoms: Pain (referred to right occiput) and headache, vomiting, vertigo, and mental hebetude. Condition of ear: Large granulation seen in meatus—ear discharging freely; temperature 98° F., pulse 54, respirations 14. Spontaneous nystagmus towards same side as lesion; slight congestion of right optic disk. Operation (April 18, 1912): Post-aural incision: pus and cholesteatoma in mastoid and antrum; exposure of lateral sinus and exploration of cerebellum between the lateral sinus and external semicircular canal; abscess containing 3 oz. of pus found and drained.

(4) *Right Chronic Suppurative Otitis Media; Lateral Sinus Thrombosis.*—E. F., female, aged 19. Right suppurative otitis media of sixteen years' duration. One week's history of acute illness: pain, mental dullness, headache, rigors, no vomiting; temperature 98.2° F., pulse 72, respirations 20. No nystagmus, ptosis, or optic neuritis. Cerebrospinal fluid: Tension raised, otherwise usual. Patient admitted about 10 p.m.; at 4 a.m. a rigor occurred; temperature 104° F. Operation (July 27, 1910): Post-aural operation: middle ear filled with granulations; mastoid contained cholesteatoma; radical mastoid emptied and then the lateral sinus was exposed. A perisinus abscess was first found, and on incising sinus wall a clot was seen; this was removed and the sinus packed. The jugular vein was not ligatured.

(5) *Chronic Suppurative Otitis Media; Labyrinthine Fistula.*—Suppurative otitis media of many years' duration. Symptoms: Dizziness, especially on syringing the ear; severe though occasional headaches; no pain. Hearing: Watch heard 1 in. from ear; tuning forks lateralized to diseased ear. Caloric tests. Positive results obtained in fifteen seconds; fistula nystagmus well marked, both on compression with bag and on pressing the tragus inwards. Condition of ear: Large perforation in posterior segment, not very active suppuration. Operation (August 17, 1910): Post-aural operation: mastoid very hard and sclerosed; necrosis chiefly confined to antrum; large fistula seen on external semicircular canal, this was left untouched and the complete radical operation performed. Vertigo complained of at first few dressings, but quite disappeared afterwards. No return of symptoms.

(6) *Temporo-sphenoidal Abscess (Right) following Chronic Suppurative Otitis Media.*—G. H., female, aged 30. Right suppurative otitis media of twenty-five years' duration. Symptoms: Pain—headache over right eye and temple (fourteen days' duration), vomiting not related to ingestion of food; temperature 99.4° F., pulse 64, respirations 18. Hearing: Watch not heard at all; tuning forks lateralized to the right side. Caloric tests negative: no "fistula nystagmus." Condition of ear: Small granulation in ear; large perforation in posterior segment; necrosis. Reflexes: Knee-jerks exaggerated; no ankle clonus; Babinski's reflex (left side). Cerebrospinal fluid: Tension raised, slightly turbid, increased polynuclear leucocytosis, slight increase of albumin, glucose 0.2 per cent. Blood count: 14,000 white cells. Operation (February 29, 1912): Post-aural operation: pus under tension in antrum; large cholesteatoma in mastoid; middle fossa exposed, dura incised and brain explored; abscess

containing 1 oz. of pus found in temporo-sphenoidal lobe, very superficial; large rubber drainage-tube inserted.

(7) *Right Suppurative Otitis Media and Extradural Abscess in Posterior Fossa.*—S. M., male, aged 6. Right suppurative otitis media of three years' duration. Symptoms: Pain in ear and over mastoid, tenderness over mastoid; mastoid periostitis—displacement of auricle; temperature 100'4° F., pulse 110, respirations 20. Condition of ear: Large polypus in right meatus; ear discharging freely. Mental condition quite normal, and no sign of intracranial suppuration. Operation (August 12, 1910): Post-aural operation; the antrum and mastoid contained broken-down cholesteatoma. On tracing a cell backwards a large extradural abscess in the posterior fossa was found, exposing a large area of cerebellum.

PROFESSOR ELLIOT SMITH gave a demonstration upon—

- (a) *Mastoid disease in Prehistoric Egypt.*
- (b) *The central auditory paths.*

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

VOLUME THE FIFTH

COMPRISING THE REPORT OF THE PROCEEDINGS FOR THE
SESSION 1911-12

PATHOLOGICAL SECTION



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1912

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PATHOLOGICAL SECTION.

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The Council think it right to state that the Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Pathological Section.

October 17, 1911.

Dr. R. T. HEWLETT, President of the Section, in the Chair.

Carcinoma of the Uterus in a Rabbit.

By ARCHIBALD LEITCH.¹

MALIGNANT tumours seem to be exceedingly rare in rabbits. Petit² records two cases, a primary carcinoma of the lung, and a carcinoma of an accessory pancreas in the omentum. Bashford³ mentions the fact of having found a carcinoma of the mamma and a sarcoma of the subcutaneous tissue, the latter being capable of propagation. I am informed by a veterinarian who has extensive post-mortem experience of rabbits and guinea-pigs that malignant disease is practically unknown amongst these animals. The above are the only cases of which I have any note apart from uterine carcinoma. Of the latter there are a few on record.

There can hardly be any doubt but that Lambert Lack's⁴ famous case was one of primary carcinoma of the uterus with metastases. He cut open the ovaries of a rabbit, scraped the raw surfaces with a knife, and allowed the milky juice containing epithelial cells to diffuse through the peritoneal cavity. The animal remained in good health for nearly a year thereafter, but at the end of that time, becoming weaker and thinner and suffering from dyspnoea, it was killed. On examination he found in the mesentery numerous hard white nodules varying in size from a pinhead to a pea, small, white, densely hard patches in the liver, infiltration of the diaphragm with projecting masses on its pleural surface, nodules on the parietal pleura and a few in the lungs; the

¹ From the Caird Cancer Research Laboratory, Dundee.

² "Travaux de la deuxième Conférence Internationale pour l'étude du cancer," 1900, p. 209.

³ Ninth Annual Report of the Imperial Cancer Research Fund, July, 1911.

⁴ *Journ. Path. and Bact.*, Edinb. and Lond., 1900, vi, p. 154.

whole mediastinum was occupied by a mass of tumour-like tissue. *The uterus was greatly thickened, the mucous membrane papilliform, and at one place in the wall there was a tumour as large as a cherry.* Microscopical examination of the nodules from various parts showed alveolar spaces lined by one or more layers of columnar epithelial cells, or entirely filled up with cells that had lost their columnar shape. It was a typical columnar cell carcinoma. Lack regarded it as having "all the characteristics of an ovarian cancer," and considered it to have resulted from the mechanical dissociation of ovarian cells which he had produced. Though the uterine tumour does not appear to have been the largest of the nodules, yet the great thickening of the rest of the uterus and the papilliform arrangement of the mucous membrane, together with the absence of any noted change in the ovaries or other sites of columnar epithelium in the vicinity, point to the uterus being the only probable source of a tumour with such histological characters.

Strangely enough, within the same year Shattock¹ reported an undoubted case of spontaneous carcinoma of the uterus in a rabbit, and was able properly to orientate the hopes that otherwise might fairly reasonably have been entertained regarding such mechanical production of malignant change. In Shattock's case there were a certain number of nodules in the peritoneal cavity; the uterine cornua were enlarged and tortuous, and contained nodular swellings reaching a maximum diameter of 3 cm. The peritoneum over the swellings was smooth. There was scarcely any area of uterine mucosa between the actual tumours that was not obviously abnormal, the membrane being papillary and cystic, though the muscular wall at these situations was not invaded. The tumours had a villous or cystic surface, and involved the entire thickness of the muscular wall. The histological appearances were those of a columnar cell carcinoma, in many places of the villous or papilliform variety.

Boycott² reported four cases of epithelial tumours in rabbits. All four were found within a few months "during the breeding season" in a series of 140 to 150 females. The first showed a solid tumour 8 cm. by 2 cm. by 3 cm. in one cornu of the uterus. It was covered with cubical epithelium, and consisted of a loose connective tissue stroma with irregular epithelial growths, mostly solid masses of cells, but with a goodly number of alveoli lined with cubical epithelium. The

¹ *Trans. Path. Soc. Lond.*, 1900, li, p. 56.

² *Proc. Roy. Soc. Med.*, 1911, iv (Path. Sect.), p. 225.

muscular coat was deeply infiltrated on the mesometric side. The other cornu of the uterus contained five foetuses with abnormal placentation. In the second case there was a single tumour mass measuring 2 cm. by 1.5 cm. Solid masses of epithelial cells and alveoli existed in equal proportions. Some of the latter were much distended, and there was a considerable amount of intra-alveolar papillary growth. The third case also showed a single uterine mass, 6.5 cm. by 2 cm. by 1.5 cm., almost entirely alveolar, with a flattened lining epithelium and a number of intra-alveolar growths. It extended into the wall of the uterine cavity over the fundus, and spread along between the deep ends of the

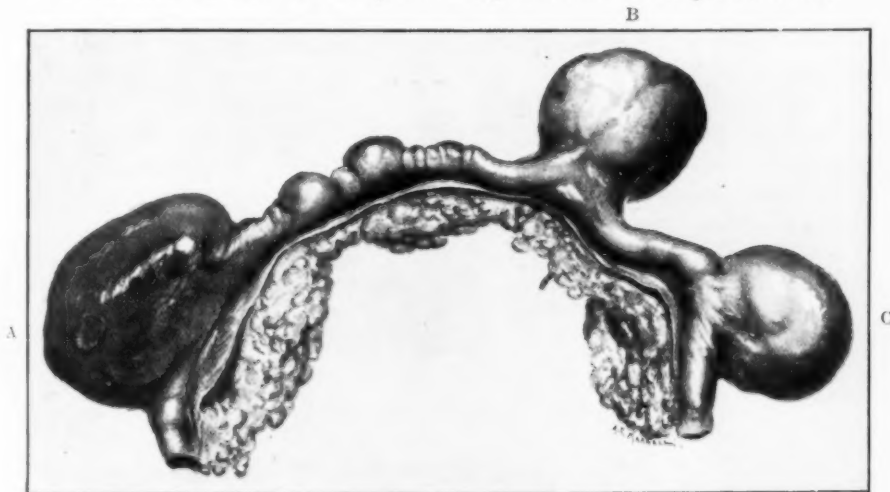


FIG. 1. ($\times \frac{3}{4}$.)

Drawing of the uterus, showing three large tumours. Tumour A, situated in the right cornu, shows a puckered area of infiltration of the serous coat. Tumour B is at the cornual junction. Tumour C is in the left cornu. Between A and B are two smaller swellings.

glands and the muscular coat. In the fourth case, one cornu contained five, the other six, small equidistant pedunculated tumours with small alveoli, some solid masses and many intra-alveolar growths. There was hæmorrhage into the stroma at one place, and some necrosis both of connective tissue and epithelium. All the tumours agreed in having a delicate stroma with a free blood supply. In the distended alveoli there were no microscopic contents. The vessels were quite large, but had simple endothelial walls of only capillary thickness. They all appeared

to have arisen mesometrically in the site of normal placentation, and Boycott suggests that they arose in sequence to abortions.

The history of my own case may therefore be of interest. We had in the laboratory for a few months a crossbred doe probably about two and a half years old. In the first week of February of this year she was mated to a buck and apparently became pregnant. She was therefore expected to litter in the first week of March, and actually did give the usual warning by plucking out the hair around the milk glands, a thing that usually happens one or two days before littering. She passed the calculated time without anything happening. The distension of the abdomen slightly diminished, and on March 21 she was again mated to a Dutch buck. The swelling of the abdomen now increased more than previously. On April 19, two days before the expected littering, she again started to pluck out hair and prepare a nest,¹ but again she passed the period without anything happening, and the swelling decreased somewhat. We thought we could detect fetuses on abdominal examination. On May 3 she was found in the morning with some blood in the cage, half a pint being in a dish. The rabbit was quite lively, but on examination we found blood coming from the vagina. The animal was chloroformed and the abdomen opened. The uterus showed three large tumours, one towards the extremity of the right cornu, one at the junction of the cornua, and a third on the left side (fig. 1). Between the first two there were two smaller moniliform swellings of the uterine wall. The largest tumour measured 5 cm. long by 3.5 cm. in height. The peculiar condition of a portion of the serous covering led me to think I might have to deal with a malignant tumour, so the animal was killed after the uterus had been removed, and a search was made throughout the body for metastases. None was found.

The uterus was opened over the largest tumour, and small portions, the size of hemp seeds, were removed from it and injected by means of a transplantation trocar subcutaneously into both flanks of four rabbits, and into the right flank only of five other rabbits. The specimen was put into the ice-chest for two days, and then several larger portions of the same tumour were inserted beneath the deep fascia or into the flank muscles of ten rabbits. Thus nineteen rabbits, all we could procure, were injected with tumour material.

¹ The fact that the rabbit on two occasions made timed preparations for expected litters which did not arrive, would seem to indicate that rabbits calculate the date of littering not from any specific internal stimulus, but by reckoning from the supposed time of conception, as human beings do. This is also borne out by observations on rabbits exceeding their term.

The uterine cornua are considerably thickened. The largest tumour (tumour A) in the right side, situated close to the extremity, bulges out the uterine wall anteriorly, posteriorly, and towards the fundus, and overhangs the uterus on both sides. The peritoneal covering, though slightly and irregularly grooved, is quite smooth and intact save for a small oval area less than 1 cm. in greatest diameter, where there is a depressed puckering with a raised margin. Internally the tumour is seen to be attached anteriorly and to the fundus (fig. 2). It is a very irregular nodular growth with some ulceration and hæmorrhage towards the centre of its surface. It is soft on section and shows an appearance like testicular substance. The central part is necrotic. The tumour infiltrates the muscular wall, and is continued through the serous coat



FIG. 2. ($\times \frac{1}{2}$.)

Uterus opened posteriorly, to show tumour A.

at the externally puckered area (fig. 1). The distended endometrium of the cavity is fairly smooth.

Tumour B, situated over the cornual junction, is spherical and pulls the uterus upwards. It is not so grooved as the former tumour, and its peritoneal coat is uniformly smooth and intact. Internally it is seen to be composed of two distinct growths which have a smooth surface. They are attached towards the fundus and the cornua open below them. The vagina is normal.

Tumour C is in the middle of the left cornu. It is the smallest of the three. Its internal surface is smooth, and like the last it does not infiltrate the muscular wall. Sections through the smaller nodular thickenings and at various parts throughout the cornua show considerable papilliform proliferation of the endometrium, through which the cavity of the uterus winds tortuously. Here and there there are solid subendometrial growths.

The portion of tumour A growing into the uterine cavity is composed of simple tubules lined with a single layer of cubical epithelium set in a delicate and relatively abundant alveolar stroma (fig. 3). Throughout the stroma run numerous thin-walled capillaries. Alveoli with simple walls predominate. Some of the spaces contain cellular debris. There are other alveoli with complicated intra-alveolar growths, and others, again, quite filled up with proliferating cells that tend to produce daughter lumina in the masses. The epithelium lining the simple spaces is cubical, though at parts more typically columnar. In the infiltrating portion of the tumour as it makes its way through the muscle we have no longer a delicate surrounding stroma, nor the regular glandular formation. Between the muscle-fibres the cell masses are very irregular and the shape of the cells distorted. Attempts at glandular formation are still seen. The muscular wall is quite broken up, and the epithelial masses come right up to and involve the serous coat (fig. 4). In this part the nuclei are not so large or round as in the free portion. In some of the masses there are areas of necrosis. Close to the serous coat there are many large blood spaces. At the edge of the tumour the unproliferated endometrium is reflected on to the surface of the tumour, separated from it at first by a thin open-meshed connective tissue, but gradually thinning out as it proceeds, till finally it disappears and the tumour cells appear on the surface.

In the other two tumours simple single-layered tubules are scarcely to be found. Many branched spaces abound, lined usually with columnar epithelium often several layers thick. At parts the alveoli are practically solid masses, although traces of glandular formation are also seen. The endometrium reflected on to the tumours gradually fades away and becomes indistinguishable from the superficial cell masses. The stroma is at parts of the same fine alveolar type as in tumour A, though at parts considerably denser, and is well supplied with thin-walled capillaries. The invasion of the muscular wall has not progressed so far as in the first tumour.

A section taken through the nodular swelling of the uterine wall close to tumour A shows a double cavity, both parts being lined by ciliated columnar epithelium. In the anterior part the endometrium is but slightly papilliform, in the posterior part it is much more exuberant. Between the two, extending from fundus to mesometrial attachment, is a mass of tissue consisting of a fine cellular stroma in which are set alveolar spaces lined by columnar or cubical epithelium with considerable infolding of the wall. All gradations are found between this and

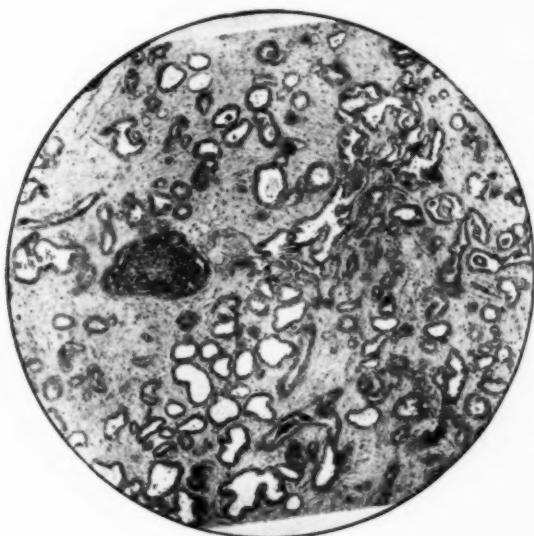


FIG. 3. ($\times 60$.)

Section of portion of largest tumour. Zenker fixation.

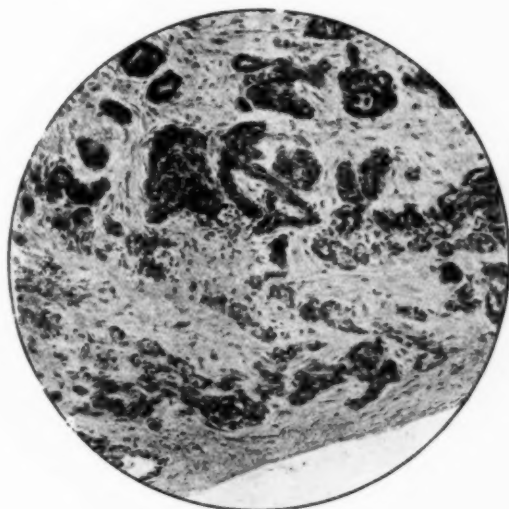


FIG. 4. ($\times 125$.)

Infiltration of muscular wall in tumour A.

the ultimate small acini with no observable lumen. Anteriorly the endometrium lies directly over the growth, posteriorly it is separated from it by a highly vascular connective tissue. Posteriorly to the second cavity there is a smaller mass of the same characters, and insinuating between the edge of this mass and the musculature of the wall can be seen a portion of the endometrium infiltrating among the muscle-fibres (fig. 5 [1]). This gives us a possible clue to the way in which the tumour masses are formed. In the next nodular swelling the cavity is also double. The endometrium is more complicated, and the axis of tumour growth extends diagonally backwards and downwards between the two portions of the cavity (fig. 5 [2]). The epithelial cells have formed themselves into solid alveoli, and the stroma is very scanty. The contrast between the papilliform endometrium with its well-marked columnar cells and the densely cellular subjacent mass is very striking. Between this last swelling and tumour B there is extreme papillomatous development of the lining membrane, splitting up the cavity into a complicated pattern (fig. 5 [3]), but there is no infiltrating growth. Between tumours B and C, and distally to C, there is the same proliferation of endometrium (fig. 5 [4 and 5]). At some parts the stroma of the papillæ is myxomatous.

The animals into which portions of the tumour were inoculated were first examined on the tenth day, and thereafter three or four times a week (fig. 6). Fourteen of the nineteen gave evidences of successful transplantation. Four of the nine inoculated with fresh tumour material on May 3 showed nodules; all those injected on May 5 with large amounts showed at first relatively larger nodules, but as there had been more laceration of tissue in the second series, and as the material injected was older, it is probable that the greater inflammatory reaction gave an exaggerated idea of the real size of the grafts. In the latter series, after this reaction subsided, steady diminution, apparently the result of absorption, was the invariable result, in some more rapid than in others. The rabbits have now been observed over a period of five months. Some have died, one was killed owing to injuries it sustained in fighting, two have had portions of their tumours removed from them and transplanted into a second generation, and of the remainder only one nodule has survived with practically no variation in size over this period of time. Whether it is wholly replaced by fibrous tissue, or still contains living epithelium, I do not know. None of the tumours showed progressive increase. My experience in transplantation of diminishing tumours in mice has not encouraged me to attempt

transplantation of these diminishing nodules in the rabbits. The sequence of events in the grafts would seem to be as follows: first, degeneration of the introduced stroma and of the more central parts of the parenchyma, and their replacement by connective tissue derived from the host, the epithelial elements towards the periphery surviving, and perhaps multiplying to a certain extent; second, an increase in the

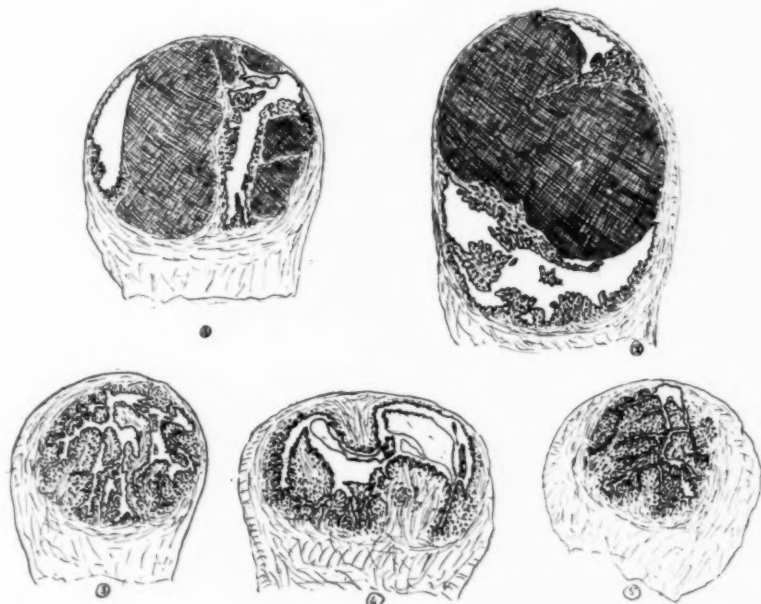


FIG. 5.

- (1) Transverse section of uterus between tumours A and B, close to A; cavity double; two apparently separate neoplasms.
- (2) Transverse section of uterus between tumours A and B, midway; cavity divided into two by an infiltrating new growth.
- (3) Transverse section of uterus between tumours A and B, close to B; marked papilliferous formation of endometrium.
- (4) Transverse section of uterus between tumours B and C; papilliferous ingrowths of endometrium; no definite invasion of uterine wall.
- (5) Transverse section of uterus distally to tumour C; excessive papilliferous formation.

fibrous tissue encapsulation of the graft with maturing and densification of the new stroma; third, cystic formation and coalescence of neighbouring acini with desquamation of the epithelial cells, a feature that is more

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marked as the graft ages; and finally, a degeneration of the remaining epithelial cells and their complete replacement by overgrowth of the connective tissue.

The nodules examined were as follows:—

(1) Young rabbit, "Sally." Injected on right flank with fresh tumour tissue. On the tenth day the nodule was about 2 mm. by 2 mm. Ten days later it measured 5 mm. by 3 mm. The animal was found dead twenty-two days after injection. The graft is surrounded by a thin capsule of young fibrous tissue, in which there are several dense collections of small round cells (fig. 7). In the centre of one of these collections there is an isolated alveolus filled up with degenerated

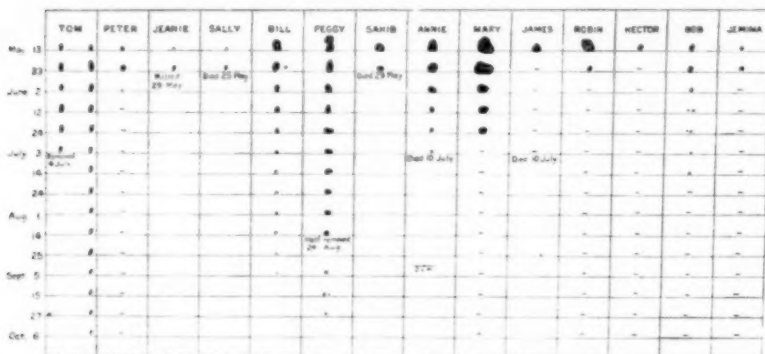


FIG. 6.

Chart of inoculated tumours. The first four were inoculated on May 3; the other ten on May 5. The distance between the upright lines is 5 cm.

epithelial cells. Fibroblastic tissue penetrates between the external alveoli at parts, and cuts them off from the others. Here and there the alveolar spaces are dilated, and the lining cells consequently flattened out. The original stroma in the centre is degenerating; the protoplasm of the cells is ragged and granular. Most of the alveoli are well preserved and healthy-looking, though all show more or less desquamation of lining cells. Lymphocytes are invading some of the epithelial cells. No polymorphonuclears are seen. Karyokinetic figures were not with certainty recognized. This nodule had undoubtedly increased in size, and the increase was not due solely to the proliferation of the tissues of the host.

(2) Young rabbit, "Sahib." Deep injection of a pea-sized portion

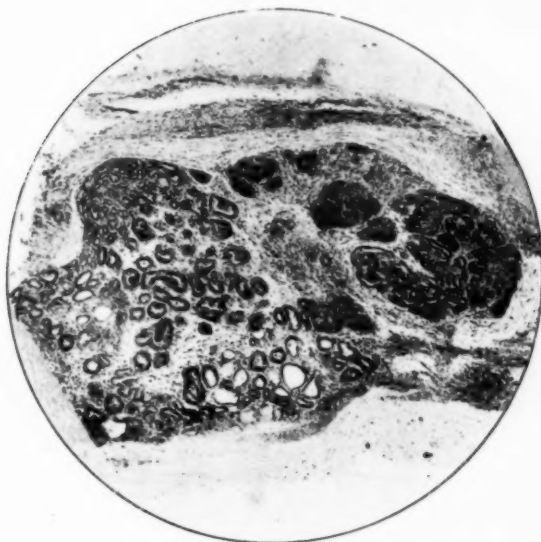


FIG. 7. ($\times 60$.)

First generation. Age of graft twenty-two days.

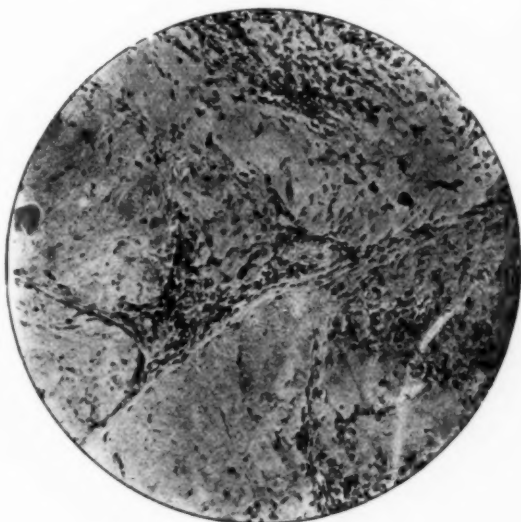


FIG. 8.

First generation. Age of graft twenty-four days.

of tumour tissue two days old. On the eighth day the palpable nodule measured 9 mm. by 6 mm. Ten days later it had decreased to 7 mm. by 4 mm. The animal was found dead twenty-four days after inoculation. The nodule was not more than 3 mm. in greatest diameter. All traces of the alveolar arrangement have been lost. A new tissue rich in capillaries has replaced to a great extent the transplanted parenchyma. Large irregular spaces of granular debris with degenerating nuclei scattered throughout represent the parenchyma of the graft. The new fibroblastic tissue has included in it the degenerating representatives of original cells of parenchyma and stroma (fig. 8).

(3) Young rabbit, "Jeanie." Injected on right flank with fresh tumour tissue. On the tenth day the nodule measured 2 mm. by 2 mm. Ten days later it measured 5 mm. by 3 mm. As the animal had its leg broken it was killed twenty-six days after inoculation. The nodule is surrounded by a thin layer of dense fibrous tissue in which are collections of round cells. Into some of these collections epithelial cells penetrate from the graft. The graft is very well preserved. In the centre there is degeneration of stroma, and to a lesser extent of parenchyma. Closely set alveoli, many of which are dilated, surround the central portion, and towards the periphery the alveoli are but little changed from their original condition. Desquamation is evident in the dilated alveoli (fig. 9).

(4) Old rabbit, "Tom." Subcutaneous injection had been done on both flanks with fresh tumour tissue. The nodules had reached a maximum of 8 mm. by 4 mm. and 10 mm. by 4 mm. respectively by the twentieth day. They then diminished to 6 mm. by 3 mm. two months after inoculation. One of the nodules was removed on the sixty-second day. It consisted of dense fibrous tissue with a softer central core. A portion of this core was retransplanted into another rabbit ("Secundus"), and the remainder examined microscopically. Enclosed in the very dense thick capsule is a relatively looser tissue containing large alveolar spaces lined by columnar epithelial cells, generally with well-defined internal margins, but occasionally ragged. Most of the spaces contain some cellular debris, and they all seem to have resulted from the coalescence of adjacent alveoli. There are clefts between the dense investing capsule and the stroma of the graft (fig. 10). The nodule on the opposite flank has persisted unchanged for five months.

(5) Old rabbit, "Peggy." Deep injection in the right flank with two days old material. On the tenth day the palpable nodule measured

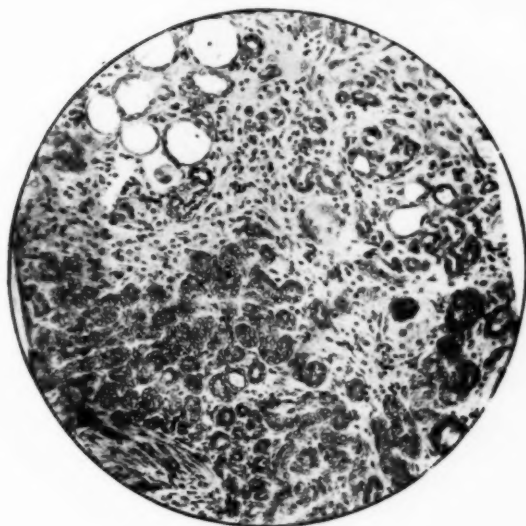


FIG. 9. ($\times 125$.)
First generation. Age of graft twenty-six days.



FIG. 10. ($\times 63$.)
First generation. Age of graft sixty-two days.

1.5 cm. by 9 mm. This steadily diminished till a size of 5 mm. by 4 mm. was reached three and a half months from time of injection. One hundred and eleven days after inoculation half of the tumour was removed; the remaining portion has now practically disappeared. A piece of the part removed was examined histologically, but shows merely connective tissue with several collections of round cells. No traces of epithelial cells are found (fig. 11). The remainder of the part removed was injected subcutaneously into two young rabbits ("Sydney" and "Francis").

A small nodule was found in another rabbit which died sixty-three days after deep injection. It had decreased from a maximum of 11 mm. by 9 mm. on the eighth day to a minute nodule about 1 mm. at the time of death. The nodule was lost in preparation. Seven other animals which exhibited nodules for varying lengths of time are still alive with no palpable evidence of them.

(6) Young rabbit, "Secundus." Injected with portion of nodule from No. 4—sixty-two days old growth. Second generation. A very minute nodule resulted. The animal died thirty-four days after the injection. The nodule consists of dense connective tissue in which are set a few irregular alveolar spaces lined by flattened cubical epithelium one cell thick. These cells are rather granular and the nuclei are not always very clear. The internal margins of the cells are seldom well defined. In addition to these there are several other spaces from which the cells have almost entirely disappeared, and round these last are dense collections of black pigment. Other masses of black pigment are found in cells between the fibres (fig. 12).

(7) Young rabbit, "Sydney." Injected with portion of tumour removed from No. 5—one hundred and eleven days old growth. Second generation. Though the portion examined from the last generation showed no trace of epithelium, yet when this rabbit of the second generation died thirty-three days after inoculation there was found in the midst of a small fibrous nodule a cystic space a little over 1 mm. in diameter lined by flattened epithelium, in which space was a considerable amount of epithelial debris.

The other animal injected with the same material at the same time showed a very minute nodule thirty-three days afterwards, composed merely of connective tissue.

Boycott thinks that the onset of the condition in his cases was associated with pregnancy. They all occurred "during the breeding season." In his first case one-half of the uterus contained foetuses, with

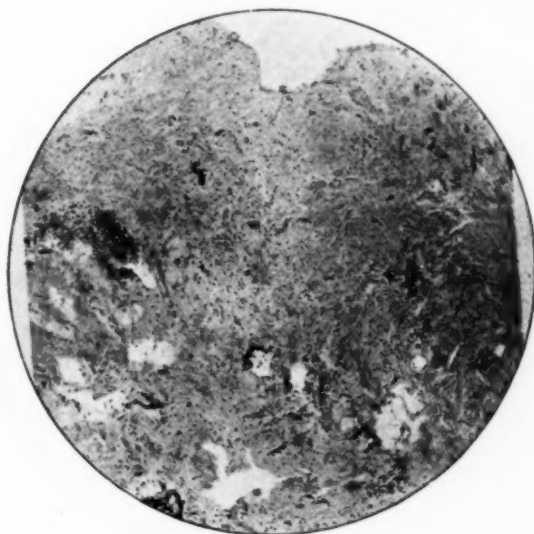


FIG. 11. ($\times 60$.)

First generation. Age of graft one hundred and eleven days.



FIG. 12. ($\times 125$.)

Second generation. Age of graft thirty-four days.

tumour formations in the other half, and all the tumours showed an attachment on the side of normal placentation. He thinks that if the foetuses came to a bad end the proliferated epithelium at the edges might grow over the depressed epithelium of the placental site, and by cutting off the latter allow it to grow and develop malignant infiltrating characters. He was unable to demonstrate any connexion between the neoplastic formation and the endometrium. In Shattock's case, as in my own, and probably also in Lack's, a very noticeable feature was the enormous papilliform proliferation of endometrium throughout the rest of the uterine cavity. Whether this general hyperplastic endometritis preceded or followed the conception is a point on which, of course, we have no information. It may quite as well have been the cause as the consequence of the foetuses coming to a bad end. But it would seem more probable that if the sequence were as Boycott suggests the proliferation of endometrium would be confined to the vicinity of the tumour formations and not be generalized over the uterus as they were in our cases. In my own, for example, the endometrium more closely approximates the normal in the immediate vicinity of the tumour. Again, the attachment of the tumours in the present case was mostly anteriorly and in the fundus in the case of the larger, and irregular in the case of the smaller, nodules. I have not been able to trace a definite unmistakeable connexion between the more or less normal endometrial epithelium and that forming the bulk of the tumours, but neither have I been able to demonstrate an epithelial covering of the larger tumours distinct from them and continuous with that of the endometrium. It is in most cases impossible in adenocarcinomata of a surface to demonstrate an unbroken epithelium from the purely simple to the undoubtedly malignant portion, though such a connexion did undoubtedly originally exist. In the smaller swellings there is a distinct endometrial covering often separated from the underlying tumour mass by a well-marked vascular stroma. But some of my sections are, I think, capable of demonstrating a connexion between tumour and endometrium, or at any rate of showing how it has arisen and been lost. From all sides of the uterus there are papilliferous ingrowths with their covering epithelium extensively folding as it proliferates. The cavity of the uterus becomes excessively complicated and the available space is filled up. An internal pressure exists, the wall is distended, and at the bases of the papillæ the proliferating epithelium is forced inwards in the submucous coat or between the separated fibres of the muscular wall. The delicate stroma of the

undoubted tumour formations is probably continuous with that of the endometrium, in which case the tumours at one stage of their history might be comparable to adenomyomata of the uterus in the human subject, which condition, as Cameron and I pointed out,¹ is midway between and has characters of both hyperplastic endometritis and adenocarcinoma. In the present case we pass insensibly from a condition of hyperplastic endometritis to infiltrating adenomatous formation. The growth of stroma lags behind the growth of gland tubules, and the growth of gland tubules lags behind the growth of individual gland cells. The same factor that started the papillomatous proliferation of endometrium is also the cause of the adenocarcinomatous formation.

As far as the history of the case goes it seems in some way to be related to pregnancy. In no part of the specimen could I detect remains of conception products nor any decidual cells in the wall or in the tumours. At no time had we any evidence of abortion having taken place. On the whole, Boycott's theory of formation cannot be ruled out, and it may quite well be that the general proliferation of epithelium throughout the uterus, which is not a normal condition in ordinary pregnancy, was the result of the stimulus of a superadded second conception. Whether the condition can be produced experimentally by interference with early pregnancies, as Boycott suggests, is a point on which I am not at present able to offer an opinion; the technical difficulties are great.

The particular portion of the tumour transplanted was histologically in that period of transition in which it is impossible to say definitely whether it is simple or malignant. The failure of the grafts to go on increasing does not prove it to have been simple, nor do I think that if, on the contrary, they had increased it would necessarily have proved that we originally started with a tumour in a malignant condition. The failure to transplant is not an evidence of the benignancy of a tumour, nor is the transplantability a criterion of its malignancy. If we had had more animals at our command at the time we might have had in some of them increasing growths capable of indefinite propagation and have been able by means of them to carry on investigations which are subject to severe limitations in laboratory animals so small as mice. As it is, we have only at the best a fragmentary study in degenerations.

¹ *Lancet*, 1904, ii, p. 84.

**A further Contribution to the Study of Rheumatism. The
Experimental Production of Appendicitis by the Intra-
venous Inoculation of the Diplococcus.**

By F. J. POYNTON and ALEXANDER PAINE.¹

THE first step in this communication is to indicate accurately the source of the infective agent with which our results were obtained.

A boy, aged 14, previously healthy and with a good family history, came to University College Hospital in August, 1911, suffering from a first attack of acute rheumatism of five days' duration. It commenced with pain in both knees and ankles, and later in the left shoulder. His temperature was 100.5° F., and pulse-rate 100 to the minute. Both knee-joints were tender and full of fluid, and the other joints named above were painful. For twenty-four hours an apical systolic murmur was faintly audible, but this disappeared, and the boy made a rapid and complete recovery. He was treated with salicylate of soda. The only point at all unusual in this case was the excess of fluid in both knee-joints, the right one being distended. Mr. C. E. Shattock, acting house physician, tapped this joint for us and a greenish fluid, which coagulated and contained some fibrinous shreds, was obtained. From this the diplococcus was isolated and grown in pure culture, and is the infective agent which we have used for the following experiments.

The animals used for experimentation were rabbits, and we would lay special stress upon the point that we used consistently for the first time young ones of some six to seven weeks of age. All the injections were made from bouillon cultures into the auricular veins.

The first animal injected with a large dose died of general pericarditis. The second was six weeks old and received $\frac{1}{2}$ c.c. of a bouillon culture. Multiple arthritis followed and mucous diarrhoea, the animal dying from an intussusception of some days' duration. In passing we would comment upon this occurrence of acute intussusception in two animals as a sequel, and possibly a result, of the infection. A pure culture of the diplococcus taken from the joint of this animal was used for the third rabbit. This was seven weeks old, and was inoculated on

¹ From the Research Laboratories of University College Hospital and the Cancer Hospital Research Institute.

September 2 with 1 c.c. of a bouillon culture. *Monarthrit*is of the left knee-joint developed, with general illness and diarrhœa; death occurred on the third day. The post-mortem showed that for 1½ in. in the middle two-fourths of the appendix there was acute inflammation. The left knee-joint showed the usual early synovitis. The liver showed fatty areas. The spleen was slightly enlarged and firm. The kidneys were not remarkable. There were no petechiæ and no post-mortem

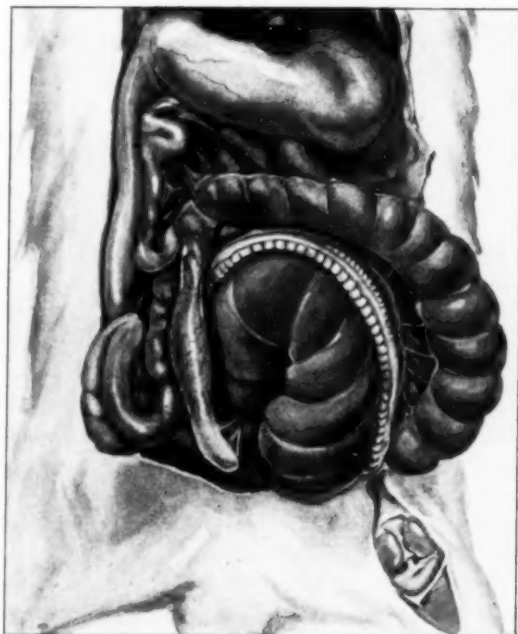


FIG. 1.

Rabbit No. 3.—The abdomen opened, showing the swollen and inflamed appendix.

staining, the heart was not opened, but there was excess of fluid in the pericardial cavity. The diplococcus was recovered in pure culture from the left knee-joint and the heart's blood. The appendix was clearly inflamed and the mucous membrane swollen and red. A small piece was excised for histological investigations.

The rabbit is shown here to-night (fig. 1) with histological sections,
x—21a

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illustrating the diseased condition of the appendix (fig. 2) and the presence of the infective agent in the blood-vessels, in the submucosa (fig. 3), and in the necrotic tissue of the mucous membrane (fig. 4). The details of this histological examination are as follows: The muscular and serous coats of the bowel are healthy, but the mucous and submucous layers show extensive necrosis. There is destruction of Lieberkühn's follicles and the lymphoid tissue. The basal vessels of the submucosa are engorged with blood, and *numerous diplococci* can be seen both in the vessels and in the tissues of the mucous and submucous coats. The *Bacillus coli* has invaded the necrotic area. Lastly, there is a slight fibrino-cellular exudation into the lumen of the gut. Although

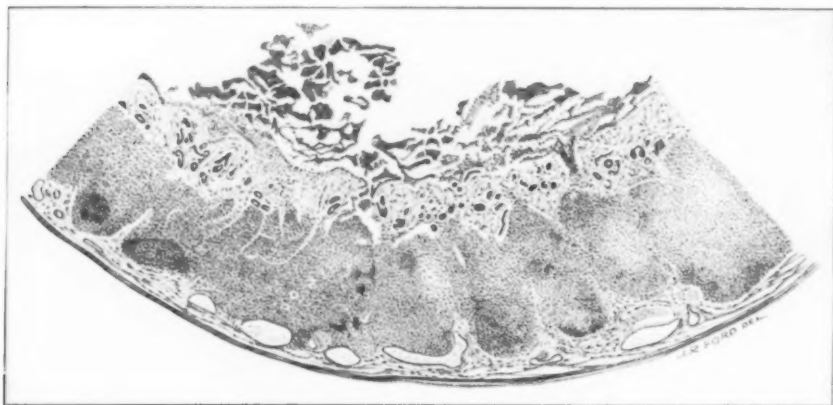


FIG. 2.

Rabbit No. 3.—Section through the inflamed area of the appendix, showing : (1) Exudation in lumen ; (2) destruction of Lieberkühn's follicles ; (3) necrosis of lymphoid follicles ; (4) dilatation of blood-vessels at the base of the submucosa.

this was the third rabbit alluded to in this paper, four others had been inoculated and developed multiple arthritis but no appendicitis, but one more in this series, that is, the fourth mentioned here, developed in addition to multiple arthritis in both elbow-, knee- and carpal-joints, some diarrhoea and was killed when *in extremis* on the fifth day. *The middle two-fourths of the appendix* showed small opaque areas, deep-seated in the substance of the wall, and this part was swollen and firm to the touch. The blood-vessels in this situation were engorged. On

opening the appendix a mucoid faecal-stained fluid escaped, and at one spot on the inner surface a reddened depressed area the size of a hemp seed was visible. The opaque areas seen from the external aspect were still more obvious from within; at the junction of the appendix with the



FIG. 3.

Rabbit No. 3.—Section showing the diplococci in a blood-vessel of the submucosa.

cæcum there was an enlarged lymphatic gland, and there was excess of fluid in the peritoneal cavity. The spleen was slightly enlarged but not soft, the liver was dark and firm and the kidneys pale. The heart was dilated and full of blood; there was no pericarditis or endocarditis.

The lungs were congested and there was excess of fluid in the pericardial cavity. A pure culture of the diplococcus was recovered from a knee-joint. The depressed area in the appendix proved to be an acute ulcer (fig. 5), a section of which is under the microscope and the histology of which was as follows: The chief changes are visible in the mucous and submucous coats. These are of two kinds, in some places there is

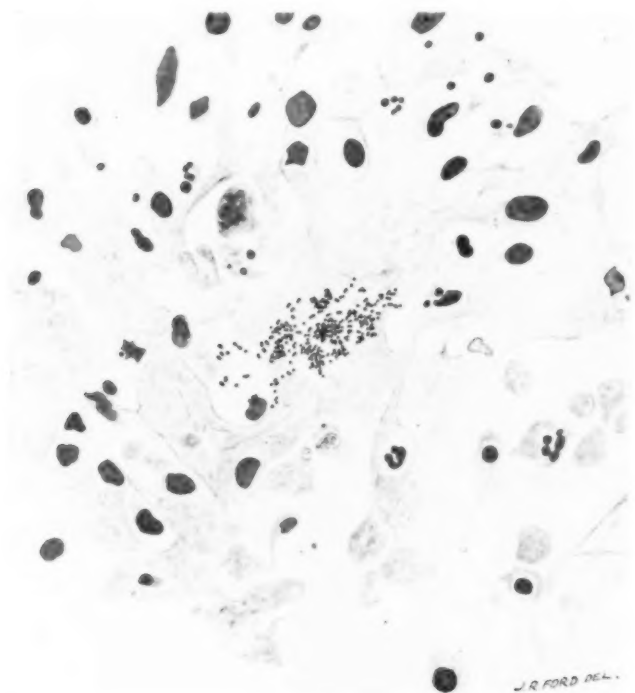


FIG. 4.

Rabbit No. 3.—Section showing the diplococci in necrotic mucous membrane.

disappearance of the lymphoid tissue with a tendency to necrosis, in others a proliferation of the connective tissue elements, pointing to the first stage towards a fibrosis. Diplococci were not demonstrated in the portion of the tissue examined, in which reparative processes were just commencing. In the area of ulceration there is local necrosis of the

mucosa and submucosa, with destruction of the epithelium of Lieberkühn's follicles and the lymphoid tissue. The muscular and serous coats are not involved and formed the base of the ulcer. The connective tissues bounding the necrotic area show commencing proliferation.

Another series of inoculations was made from the culture taken from the first rabbit which had suffered from acute appendicitis, and one of this series was killed when *in extremis* on the third day. During life, arthritis of both knee-joints had shown itself and there was some diarrhoea with general illness, the result of the inoculation. On opening the abdomen a condition was observed which we must ask you to accept

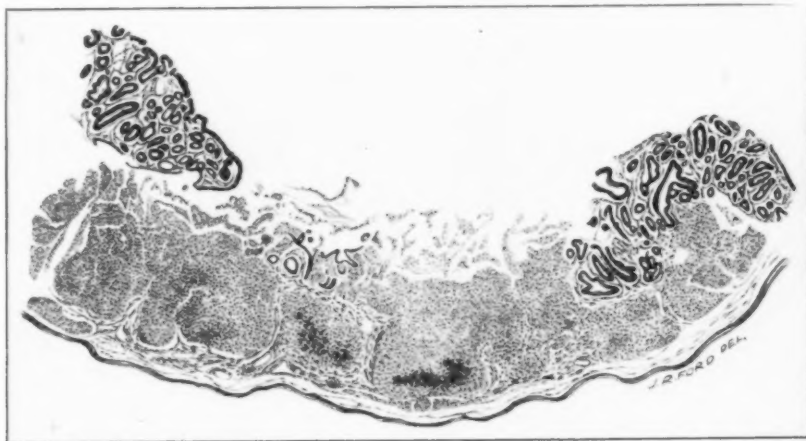


FIG. 5.

Rabbit No. 4.—Section through the wall of the appendix, showing the formation of an ulcer.

from our account, because in the process of preservation it could not be produced. We have illustrated it by means of a diagram (fig. 6). The *middle two-fourths of the appendix* were ballooned, and in the walls were small opaque areas not so extensive as in the preceding case, and situated chiefly along the mesenteric attachment. The viscera showed no noteworthy features and both knee-joints were in a condition of early arthritis. The diplococcus was recovered from one of these in pure culture. The histology of this condition shows the earliest stage of an infection by the blood-stream (fig. 7). The first changes appear in the mucous and

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submucous layers, but chiefly in the lymphoid follicles of the latter. Small foci of polynuclear cells can be seen here and there surrounding the minute blood-capillaries, and every stage of inflammatory change can be traced up to complete destruction of the normal tissue, ending either as necrosis or connective tissue proliferation (fig. 8). Diplococci are visible in various stages of destruction within the phagocytic cells, according to the stage of inflammatory reaction (fig. 9).



FIG. 6.

Rabbit No. 5.—Diagram showing ballooning of the appendix, the result of local infection of the wall by the diplococcus.

The last series that have been inoculated consisted of three young rabbits seven weeks old, which were intravenously injected on October 6 with very small doses (0.25 c.c. and 0.1 c.c.) of a bouillon culture from the knee-joint of the preceding rabbit with appendicitis. All suffered from arthritis, and one from diarrhoea, and this one died on the ninth day. There was marked arthritis of the left carpal joint and slight of

both knee-joints, the synovial membranes of which were red and congested. About $\frac{1}{2}$ oz. of turbid fluid was removed from the peritoneal cavity, and the serous membrane showed early inflammatory changes. The appendix at the junction of the last fourth with the first three-fourths showed an opaque area deeply seated in its walls (fig. 10). The blood-vessels were congested. As regards the other viscera there was no noticeable feature except that the spleen appeared to be unusually small. Cultures from the left carpal joint and peritoneal fluid gave a pure growth, and films also showed the diplococci. We would emphasize the absence of the *Bacillus coli* in the films and cultures

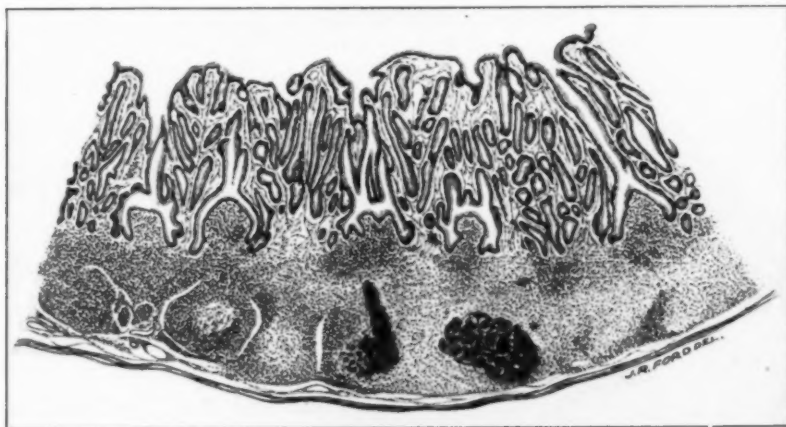


FIG. 7.

Rabbit No. 5.—Section through the wall of the appendix under low magnification. Lieberkühn's follicles are not damaged, but areas of necrosis are visible in the lymphoid follicles of the submucosa.

of the peritoneal fluid. Thus it will be recognized that in this case, which had lasted nine days, some peritonitis had occurred and the living micrococci were present in the peritoneal fluid.

SUMMARY.

To summarize our histological results, we would point out the occurrence of (1) a very early appendicitis, (2) a very severe appendicitis, and (3) the formation of an ulcer as the result of a local deposit

of the diplococcus intravenously injected. We would also express our belief that in human appendicitis, apart from the complicating event of a concretion which we know is not a constant occurrence—the histological changes might be well explained by our results. The early cases with their deposits in the submucosa and mucosa showing cell proliferation and little necrosis, might well, if they had been prolonged

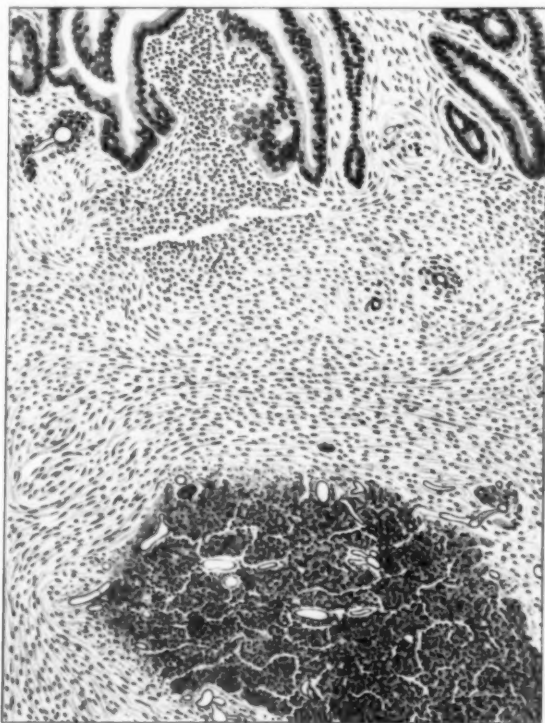


FIG. 8.

Rabbit No. 5.—Section through the wall of the appendix under high magnification, showing necrosis of lymphoid tissue and perivascular exudation.

in duration, have produced sclerosis of the wall such as occurs in chronic human appendicitis. The acute case with much necrosis would represent the virulent human condition. Lastly, the ulcer, had it healed and been rather more extensive, would have produced the stricture so often seen in man.

The rapid destruction of the diplococci by the tissues is a most interesting event, fully bearing out our previous experiences as to this micrococcus, which have led us so repeatedly to explain the difficulty of its isolation during life.

The enlargement of the lymphatic gland at the base of the appendix is paralleled in human appendicitis.

In none of these cases or in the twenty-four rabbits inoculated in this research was there a single abscess in the viscera. In so far as these results are the outcome of infection with a micro-organism obtained during life from rheumatic arthritis, and a micro-organism, too, capable

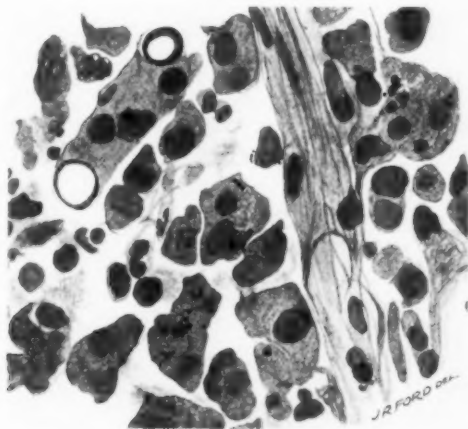


FIG. 9.

Rabbit No. 5.—Section through an inflamed area, showing destruction of the diplococci within the tissue cells.

of reproducing a similar arthritis, they are, we believe, a new contribution to the subject of experimental medicine and a new fact in the pathology of the important condition of appendicitis. If, however, we were to claim that the wider question of the possibility of appendicitis arising as a local result of a general blood infection had not been realized and experimentally investigated before, then we should do a gross injustice to others. Absolutely independent as these investigations of ours have been, we must refer to Adrian's paper published ten years ago upon the occurrence of appendicitis, both clinical and experimental, as a result of general infection. This author, in a masterly investigation, refers to

this production of appendicitis in rabbits by the intravenous injection not only of streptococci, but also staphylococci, typhoid bacilli, pneumococci, and the *Bacillus coli*. In the investigation with the pneumococcus he demonstrated the micrococcus in the wall of the appendix, and his microscopic section of the inflamed appendix resulting from a streptococcus infection, the figure of which we throw on the screen, is in accord with the histological results that we have shown to-night. He gave no details of the formation of an ulcer, or of another lesion such as arthritis, or of the condition of the peritoneal fluid, nor does he mention the source of the streptococcus, but these points are of secondary importance with regard to the general question with which his contribution was concerned.

In his paper Adrian gives many references to the work of others upon the general question of the origin of appendicitis from a general blood infection or local injury. Roux and Josué, Roger, Beauserrat, de Rouville, Gouget, and others have investigated in various ways upon this question and Adrian's paper in the *Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie*, 1901, vii, p. 407, reviews this work.

We would make the following concluding observations:—

(1) There seems to us no doubt that in these cases acute appendicitis resulted directly from an intravenous inoculation of a diplococcus obtained during life from an acute rheumatic arthritis, and it appeals to us as interesting that it was the only obvious alimentary lesion, a point which Adrian noted in his cases.

(2) The conditions that were produced were of varying severity.

(3) In each case the animal was young; heretofore, we have not observed such a condition in the older animals. This may, or may not, prove to be an accurate observation.

(4) The condition arises without the presence of any concretion or foreign body in the appendix and commences deep in the wall of the appendix. This militates, in our opinion, against the view held by Aschoff that in human appendicitis this disease starts within the lumen of the appendix.

(5) It is interesting that the middle part of the length of the appendix is affected, a position in which a stricture is so often found in man.

(6) In one case early peritonitis with living diplococci in the peritoneal fluid occurred, although there was no perforation—a point of much importance in its bearing upon the pathology of human appendicitis.

(7) The ballooning of the affected area of the appendix in one case suggests the probability that in man some such loss of tone favours stagnation of secretions and contents, and the formation of a concretion.

(8) The association of arthritis, mucous diarrhoea and appendicitis is of interest in its bearing upon the difficult question of auto-intoxication from the bowel in the human subject as a cause of arthritis. It suggests that rather than this being the primary factor, the probability is that all the lesions may be the result of some primary cause circulating in the blood-stream and determining to these various positions.

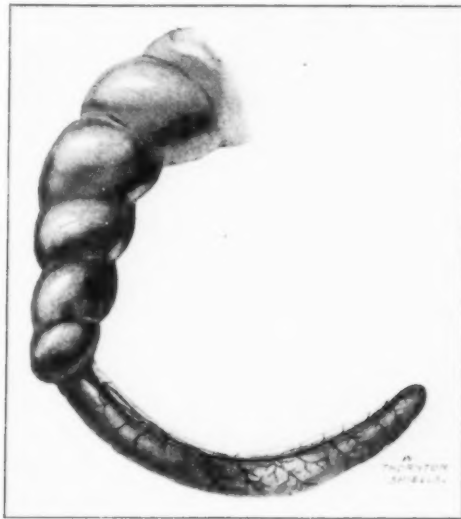


FIG. 10.

Rabbit No. 6.—Showing a pale area surrounded by congested vessels, the result of acute appendicitis.

(9) We do not assert for one moment that the only cause of appendicitis is this diplococcus. Adrian's investigations and those of others are sufficient evidence, quite apart from clinical experience, to prevent us falling into this error.

(10) Whether or not these results favour the widely held view of a relationship between acute rheumatism and appendicitis must depend upon the significance that is attached to this diplococcus and the degree of parallelism that exists between human disease and experimental infection.

**An Organism obtained from an Abscess in the Neck
of a Bullock.**

By J. BURTON CLELAND.¹

THE following is a description of a Gram-negative bacillus obtained from pus from an abscess in the neck of a bullock. The exact relationship of this organism to other well-known groups seems doubtful, but it appears connected on the one hand with the *Colon-typhoid* group, on the other with the *Bacillus pyocyaneus* group, and still again with the *Proteus* group. Of most interest, perhaps, are the varying reactions it gives on sugars, and even on the same sugar, producing in some cases acid alone, in other cases acid and gas, and still in other cases no alterations. This organism has only been fully worked out in the case of one affected animal, although it was probably obtained some months previously from a similar situation—viz., a large abscess in the neck of another bullock. In this latter an organism was isolated which presented certain features of resemblance to the typhoid bacillus in that it was a Gram-negative organism which gave acid on glucose and mannite, had no action on dulcitol, lactose, or cane sugar, and produced slight acidity on litmus milk, and as far as investigation went at the time, thus conformed with the typhoid group. Though the organism was put aside to be investigated more fully later on, it was unfortunately mislaid, so that there was no opportunity of comparing it with the one now under review, with which it conformed as far as the investigations went.

The animal, the subject of this note, was suffering from a chronic abscess in the neck. Pus was forwarded from Narrabri, where the animal was killed. It must be here noted that the possibility of the organism being a contamination cannot with certainty be excluded, and that it is only the analogy with the previous case, in which the abscess, unopened, was submitted from a local bullock, and in which a similar organism was obtained, that makes it seem probable that in the second case the bacillus was also in the unopened gland.

Smear preparations of the pus did not reveal the presence of tubercle bacilli. There were noticed a few slender Gram-negative bacilli.

¹ From the Government Bureau of Microbiology, Sydney.

Cultures were made on agar, and a number of small white colonies developed, all of which, except one, consisted of the organism in question, the remaining one consisting of Gram-positive cocci. The colonies thus isolated—in some cases repeated more than once to ensure freedom from contamination—were tested on various media, including milk, gelatine and various sugars.

Reactions on Milk.—There was no change in one day; in eleven out of twelve cultures in three days acid was produced; in the twelfth there was clot and decolorization in seven days. The upper quarter inch of the milk tubes showed the presence of a proteolytic process which slowly and gradually, after many weeks, extended throughout the tube so as to form a dirty straw-coloured fluid with some shreddy clots.

Gelatine.—Inoculation of gelatine tubes, followed by one day's incubation, and then stored at room temperature, showed in two days the presence of liquefaction a quarter of an inch from the top. The process of liquefaction gradually extended until at the end of a number of weeks the gelatine was completely liquefied, and assumed a reddish-brown tint which in certain lights gave rise to the suspicion of a reddish-yellow fluorescence.

Sugar Media.—The reactions in sugars were most disconcerting, as already mentioned. For instance, on glucose, acid and no gas was produced in some of the strains even after several days' incubation, and yet these very same strains on other occasions produced sometimes acid with a little gas, sometimes acid with much gas, and then have again reverted to acid alone. Similarly with mannite, acid was sometimes produced alone, sometimes with little gas, and sometimes with much gas. On dulcitol no change occurred. On lactose, as a rule, no change occurred, and in some instances acidity was produced after a few days. On saccharose, acidity was produced, and sometimes, after several days, small or large amounts of gas. On dextrine, as a rule, no change occurred; in some strains acid was produced, and in all of these, in several days, a little gas. On inulin, acid was produced in some strains, no change in others. On salicin, acid, and later gas, were produced. On arabinose, acid, and later gas. There was no change in adonite. Indol was not formed. The growth in peptone water was turbid and without a scum.

Cultures of the organism were inoculated into a calf, but no abscess formation followed within three weeks.

The points of special interest about this organism consist first of all

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in its relationship, as tested by reactions in culture media, to other groups of organisms, and secondly in the varying reactions in sugar media.

ITS RELATIONSHIP TO OTHER ORGANISMS.

The Colon-typhoid Group.—Morphologically the bacillus was Gram-negative, and its growth on agar was such as might well conform to an organism of this group. In fact the organism obtained from the first case was provisionally referred to this group on account of its producing acidity without gas on those sugars in which the typhoid bacillus behaves similarly. Unfortunately this organism had not been tested fully on gelatine or milk. The sugar reactions, though so changeable, are still of a kind produced by members of this group, but I am not aware that any particular member produces sometimes acid on a sugar, sometimes acid and gas, and sometimes no change. Its peptonizing effect on milk and its liquefaction of gelatine with comparative rapidity at once remove it, however, from the colon-typhoid series.

The Pyocyaneus Group.—In testing a number of organisms of the pyocyaneus-fluorescens group I have not found, as a rule, any changes in the direction of acidity, or acidity and gas in glucose, mannite, saccharose, or lactose. Occasionally in glucose acidity is produced by some of the members, but the usual change is a discharge of the litmus colour. The organism in question differs, therefore, in sugar reactions from this group, but resembles them in the way in which it affects milk and gelatine, in both cases altering these from the surface downwards. It is interesting to note that in old gelatine cultures, when the gelatine was completely liquefied there was a certain amount of colour formation which had a suspicion of fluorescence.

The Proteus Group.—Various members of this group have been tested by my colleague, Dr. Bradley, who found that some members produced acid and some acid and gas in certain sugars. Milk is digested and gelatine is liquefied with moderate rapidity. The common proteus grows as a moist film over the surface of a solid medium, which this organism does not do.

In these comparisons it would appear that the organism we are dealing with is most closely related to the group of *Bacillus pyocyaneus*, although it has some affinities with the colon group (especially to the slow gelatine liquefier, *Bacillus cloacæ*), and with the group to which the proteus belongs. Unfortunately in the present stage of bacteriology a vast number of organisms have been described, but there has been

very little attempt at a scientific arrangement into families and genera. Surely it is time that bacteriologists as a body should evolve some recognized scheme by which individual workers could, with a fair amount of certainty, assign a number of the organisms they meet with to some particular family, if not to a definite genus.¹

The Muci-carmin Staining Method.

By PERCIVAL P. COLE.

MUCI-CARMIN attracted but little attention as a means of investigating cancer until Mr. Sampson Handley suggested its use, and adopted it, to trace the spread of carcinoma in the rectum and large bowel. To be of practical use it is necessary that the results obtained shall be certain and accurate. The fulfilment of these qualifications can be easily ensured. The following details as to technique are the result of considerable experience with the stain, and are given in response to several inquiries. Several of the points hereafter emphasized have been, I find, set forth by Meyer, who introduced and described the staining method, but the conclusions have been arrived at quite independently. The stain is prepared as follows (quantities given in several books dealing with stains): Take carmine, 1 grm.; aluminium chloride, $\frac{1}{2}$ grm.; distilled water, 2 c.c. These should be thoroughly mixed with a glass rod in a small glass beaker a little larger than an ink-pot. This type of vessel is chosen because, in applying heat to such a small quantity of liquid, unnecessary evaporation is prevented if the receptacle be deep in proportion to its content. If a flattened dish be used it is difficult to avoid drying and charring. The mixture is then heated on a hot sand-bath which has been prepared beforehand. A sand-bath is preferable to a flame because the heating is more easily controlled and the necessary stirring is facilitated. The heating should be gradual and the mixture should be constantly stirred. As more and more heat is applied a curious change takes place. The mixture until now bright red suddenly becomes quite dark and seems to "flux." The steam rising from the mixture acquires a characteristic pungent odour. These occurrences

¹ *Editor's Note.*—The author's attention may be directed to the papers by Mary Hefferan (*Centralbl. f. Bakt.*, Jena, Abt. ii, 1904, xi, pp. 311, 397, 456, 520) who discusses very fully the variations in the sugar-fermenting properties of chromogenic organisms.

indicate that the proper reaction has taken place and the heating may now be stopped. Better results are, as I think, obtained by keeping the mixture gently steaming for two or three minutes longer. Alcohol of strength 50 per cent. is now stirred in, and the mixture so obtained is finally transferred to a larger vessel and diluted with 50 per cent. alcohol to 100 c.c.

This solution should stain mucus brilliantly in ten minutes, and if it does not do so it is useless. The solution may be used as it stands or be still further diluted. If an undiluted solution be used the connective tissues tend to become stained and the blue coloration of the nuclei to become faint, thus spoiling the contrast. Under these circumstances the stain should be diluted with tap-water from 1 in 2 to 1 in 6, the dilution being regulated by the condition of the nuclei, which should be "blued" by immersion in the mucicarmine mixture. Staining takes place with a strength of as little as 1 in 10, but as a rule more time is required than with the stronger solutions.

Meyer [1] suggests that sometimes a dilute solution (1 per cent.) of sodium bicarbonate may be added to counteract the free acid in the mixture, but I have never found this necessary.

The aluminium chloride must be absolutely fresh and distilled water should not be used as a diluent. The stain may need to be filtered after a few days. The stain being made, is utilized as follows:—

Fixation.—In my hands perchloride of mercury in a saturated solution, with the addition of glacial acetic acid five parts per cent., has given the best results. The tissue is placed in this fixative for three hours, washed in water half an hour, and then transferred to 50 per cent. alcohol and dehydrated and imbedded in the usual way. There is no necessity to treat tissue or sections with iodine, for no deposit occurs. If iodine be used, it is better to wait till all the staining has been done. Formalin in normal saline gives good results. Spirit fixation gives moderate results but is, in my experience, the least valuable. Zenker's solution cannot be used.

Staining.—The mucicarmine can be used first, but it is better to employ it after the nuclei are stained. Many nuclear stains have been tried, but Ehrlich's acid hæmatoxylin is the best. Stain in this for five to ten minutes. Wash in distilled water and transfer to the mucicarmine solution for ten minutes. Wash off mucicarmine with water, differentiate with acid alcohol if necessary, and "blue" again in water. The section is now ready to mount. The stain appears to keep indefinitely. A stain which was made in February, and diluted to

1 in 4, has been kept at the same volume by the occasional addition of a little water and is now staining as well as ever. The sections stained nine months ago and mounted in balsam preserve their original colouring. Fresh tissues, as might be expected, give the best results, but post-mortem and museum material stains well.

The sections exhibited were taken from the following sources:—

(1) Museum specimens of carcinoma of the colon from University College Hospital. For access to these I am indebted to the kindness of Mr. Barker and Mr. Lawrence.

(2) Post-mortem specimens of carcinoma of the colon, rectum and stomach from the Cancer Hospital. By the courtesy of Dr. Kettle.

(3) Fresh specimens of carcinoma of the colon and rectum, removed by Mr. Sampson Handley, Mr. Charles Ryall, Mr. Ernest Miles, Mr. Jocelyn Swan, and Mr. Tyrrell Gray.

(4) A fetal rectum kindly obtained for me from Queen Charlotte's Hospital by Dr. Bannister.

REFERENCE.

- [1] MEYER, PAUL. "Ueber Schleimfärbung," *Mitteil. a. d. Zool. Stat. z. Neapel*, 1897, xii, p. 317.

Experiments made with a Sarcoma-producing Mouse Carcinoma to ascertain whether the Tumour, when killed by drying, will incite a Sarcomatous Growth in the Host on being introduced beneath the Skin.

By S. G. SHATTOCK and L. S. DUDGEON.

THE observations of Ehrlich and Apolant,¹ that certain mouse carcinomata on being grafted into a further series of mice are replaced by sarcomatous formations, have been amply confirmed in this country by Russell.²

¹ Ehrlich and Apolant, (1) "Beobachtungen ueber maligne Mäusetumoren," *Berl. klin. Wochenschr.*, 1905, xlii, p. 571; (2) "Weitere Erfahrungen ueber die Sarkomentwicklung bei Mäusecarcinomen," *ibid.*, xliii, 1906, p. 37. Apolant: (3) "Die epithelialen Geschwülste der Maus," *Arb. a. d. König. Inst. f. exp. Therap. zu Frankfurt-a-Main*, Jena, 1906, i, p. 7; (4) "Ueber die Genese des Carcinoms," *Histologischer Teil, Verhandl. d. deutsch. path. Gesellsch.*, Jena, 1908, xii Tagung, p. 3; (5) "Ueber künstliche Tumormischungen," *Zeitschr. f. Krebsforsch.*, Berl., 1908, vi, 2, p. 251.

² B. R. G. Russell: "Sarcoma Development occurring during the Propagation of a Hemorrhagic Adenocarcinoma of the Mamma of the Mouse," *Journ. Path. and Bact.*, Camb., 1910, xiv, pp. 344-378.

The theoretical difficulty of explaining such a result on the assumption that the epithelial cells of the grafted carcinoma furnish the cells of the sarcoma is so insuperable that the only way of evading it would be to regard the grafted tumour as an endothelioma in place of a proper carcinoma. The transformation of epithelial cells into connective tissue is a phenomenon which is unknown, at least after the conclusion of embryonic development; whereas the same transformation of endothelium, seeing that the latter tissue is of mesoblastic source, does not present the same difficulty; the fibroblasts produced in the organization of an intravascular thrombus are derived from the proliferated endothelium of the vessel.

The apparent transformation, however, offers no histological anomaly, and the assumption that such tumours are endotheliomata is unnecessary in explanation of the result; for the simple reason, that the process is one not of transformation but of substitution.

As Dr. Russell has shown, the sarcomatous growth arises not from the graft, but from the connective tissue of the host, the proper carcinomatous cells of the graft eventually disappearing. By killing a series of mice, simultaneously inoculated, at different dates, all the stages of substitution may be traced.

It will appear from these observations that in the case of certain mouse carcinomata, some peculiar change is set up by the carcinoma cells, which stimulates the connective tissue of the host to proliferate, and produce a sarcoma.

The following experiments were undertaken in order to ascertain whether the sarcomatous reaction could be induced by the subcutaneous injection of sarcoma-producing mouse carcinoma, after the latter has been killed by drying, with the object of determining whether the result is attributable to the action of chemical substances extracted from the dead cells, or whether the cells must be living in order to bring it about.

DETAILS OF THE EXPERIMENTS.

The tumours used throughout the following experiments were sub-grafts of that numbered 100 at the Imperial Cancer Research Laboratory, and we have to thank Dr. E. F. Bashford, the Director, and Dr. B. R. G. Russell, for kindly supplying us with the material for inoculation. The tumour in question regularly gives rise to sarcomatous substitution, a fact proving that the result is not attributable to idiosyn-

crazy on the part of the mice inoculated, but to some peculiar character of the tumour itself.

When the grafts are examined up to the sixth week, they are found to consist chiefly of epithelial tissue; from the seventh to the ninth week, substitution is in progress; at about the sixteenth week, it is complete. From the pure sarcomatous tumour finally resulting, an unmixed sarcoma may be propagated by subgrafting.

The original tumour was a carcinoma of the mamma; and, as just stated, in the first steps of its growth it is as cellular, or provided with as scanty a stroma, as other mammary carcinomata in the mouse; it cannot be classed as a carcino-sarcoma, and the sarcomatous growth that results cannot be viewed as due to the growth of the stroma of the graft accompanying the disappearance of the epithelial cells.

Experiment I.

March 23, 1911: Two mice were killed thirty-three days after subcutaneous inoculation with a subgraft of tumour 100. The tumours were removed with sterilized instruments, and minced with fine scissors into a pulp, which was thinly spread over the bottom of a Petri dish and dried at 37° C., with the cover off, and shielded from light.¹ The drying was completed in one and a half hours. The dried material was then moistened with sterilized salt solution, and remade into a pulp, of which 0.05 c.c. was injected subcutaneously, with a Bashford syringe, into each of twenty mice. The animals were examined, and the results charted at the Imperial Cancer Research, on the tenth day, and after that every seventh day, according to the regular practice there adopted.

June 16: At this date, over three months after the inoculation, sixteen of the mice were alive. In none was there any growth at the site of the grafted material, nor did the charts show that any growth had at any time taken place.

This experiment was repeated on April 20, when six mice received 0.05 c.c. of material obtained from two mice inoculated on March 2, the drying of the material being completed in one and a half hours. No tumour had appeared on June 26, nine weeks after the inoculation, and the animals were then killed.

¹ Fuller details of the technique may be found in our paper on "Experiments with Air-dried Mouse Cancer." *Proc. Roy. Soc. Med.*, 1911, iv, (Path. Sect.), pp 73-86. This method of drying effectively kills the cells, without allowing time for autolysis to occur.

Experiment II.

April 20: In the following experiment the injections of dried carcinoma in place of being made only once were repeated on four occasions, with the object of prolonging its local action, and the amount introduced after the first injection was doubled, for the same purpose. Two mice which had been grafted with tumour 100, on March 2 (forty-nine days previously), were killed, the growths being removed and prepared as already described; the drying of the pulp occupied one and a half hours. Six mice were injected subcutaneously on the right side, each receiving 0.05 c.c. of the dried material remade into a pulp with salt solution.

April 27 (second injection): Two mice inoculated with tumour 100 on March 16 (forty-two days previously) were killed, the tumours being prepared as before; drying was completed in one and a quarter hours. The six mice received a second injection on the same side as before, the material being injected locally—i.e., without being distributed by withdrawing the cannula during the process of injection; and twice the amount being used—viz., 0.1 c.c.

May 12 (third injection): The procedures were repeated precisely as on the previous occasion, the injection being made into the same region. The tumours used were obtained from two mice, the drying of the pulp being completed in one hour.

May 26 (fourth injection): The injection was repeated as on the two previous occasions. The tumours used were from two mice inoculated on April 6; the drying of the pulp was completed in an hour.

August 15: None of the animals showed any tumour growth at the site of the inoculations: nor had they done so at any time during the course of the experiment. They were to-day killed.

The foregoing experiments show that for the incitement of the sarcomatous growth in the host the action of the living carcinoma cells is necessary; that the access to the circumjacent connective tissue, of the materials extracted from the cells is not sufficient, at least in the amount furnished by the method employed. The comparatively small size attained by the tumours of the particular strain used made the preparation of a salt solution extract for the purpose of injection impracticable.

The results in their general character fall in line with those which show that the action of the *living* cells, whether of carcinomatous epithelium or of normal tissue, is indispensable in the production of prophylactic immunization to the growth of engrafted carcinoma.

Pathological Section.

November 21, 1911.

Dr. R. T. HEWLETT, President of the Section, in the Chair.

The Auriculo-ventricular Bundle from a Case of Heart-block.

By W. LANGDON BROWN.

A MAN, aged 39, was admitted to the Metropolitan Hospital on October 15, 1907, with the history that he had been in his usual health until fourteen weeks before, when he began to suffer from numbness of the extremities and headaches. He was easily fatigued on the slightest exertion. There was nothing of importance in his past or family history. He was married, the father of seven children, and his wife had had no miscarriages. He was found to be well nourished, and of a good colour. Except for some lateral nystagmus his nervous system was normal in all its reactions. His chest was emphysematous, so that the apex-beat could not be seen or felt, and the area of cardiac dullness was diminished. The heart-sounds were rather faint, but there was no murmur. His pulse was 80 and regular; the systolic pressure was 120 mm. The urine was free from albumin.

Three days later he complained of epigastric pain and tightness across the chest. He said that he could feel something "jumping inside his chest." The frequency of the radial pulse was now found to be only 20, while the frequency of the venous pulse in the neck, which was very marked, was 80. A soft systolic murmur could now be heard at each contraction of the ventricles. On the X-ray screen 32 auricular contractions were counted to 9 ventricular. The dissociation of rhythm was strikingly visible. He was given strychnine and caffeine, when a normal rhythm soon returned. Two days the drugs were discontinued; within fourteen hours he had another attack. "Everything in the room was turning round," he said, and he was evidently in great

40 Langdon Brown: *Auriculo-ventricular Bundle in Heart-Block*

distress. The pulse at the wrist fell to 16, while the venous pulse was 90. He was given strychnine subcutaneously and caffeine by the mouth. Again improvement rapidly followed.

On December 14, after about three weeks' freedom from attacks, he had a series of very severe ones. At 11.15 p.m. he turned suddenly pale, his eyes rolled upwards, and consciousness was greatly impaired. The pulse at the wrist was only 15 per minute, while that in the veins of the neck was 120. Occasionally the radial pulse would increase in frequency to 80, and the patient would appear to be all right again. These intervals would last for about five minutes. Then the pulse



FIG. 1.

The degenerated fibres of the auriculo-ventricular bundle, surrounded by fibrous tissue.

would become infrequent again; the muscles, including the sphincters, became relaxed, consciousness was completely lost. The pupils were widely dilated, and the skin was bathed in perspiration. The patient went on in this condition until 11 a.m. on December 15, when the pulse became imperceptible and respiration ceased. Artificial respiration was performed and the galvanic battery was applied to the præcordium. The pulse immediately returned at the wrist and the colour improved, and a few minutes afterwards he began to breathe naturally again. He

then became very noisy and passed into an epileptiform state, in which he bit his tongue, lost control over his sphincters, and threw his arms about, while his legs and back were quite rigid. This condition lasted for about an hour, at the end of which his pulse again became imperceptible. He was revived by an injection of 10 minims of adrenalin chloride solution into the median basilic vein, and a grain of caffeine sodio-salicylate hypodermically. For about three days he passed through these phases in turn; the ventricles stopped, he became unconscious; the pulse revived, he became convulsed or excited. On several occasions

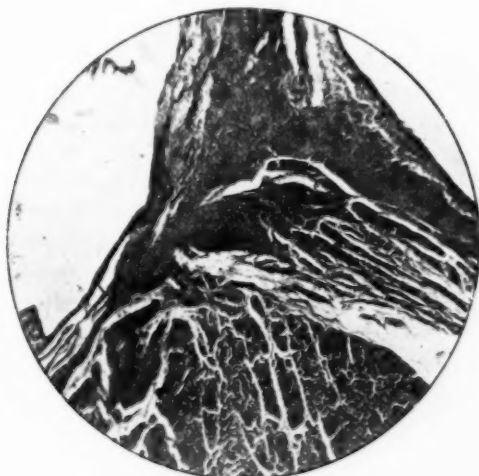


FIG. 2.

Section through the bundle of His at the lower part of the pars membranacea septi, where the bifurcation of the bundle occurs. The branch to the left ventricle can be seen running down towards the right side of the picture. The invasion of the bundle by fibrous tissue from the pars membranacea can be clearly seen.

competent observers believed him to be dead, yet on powerful stimulation the heart could be made to go on again, and he came back to life. At last it stopped for ever.

Digitalis was given on only one occasion, when 3 minims of the tincture were administered, without causing an attack. I much regret that no graphic record was taken of the venous pulse, but the X-rays left no doubt of the existence of heart-block.

The post-mortem examination was made by Mr. E. H. Shaw, Pathologist to the Hospital. He found some œdema of the brain, and some congestion of its blood-vessels. Otherwise the brain appeared quite normal; there were no visible signs of disease in the hemispheres, pons, medulla, or cerebellum. The lungs were normal except for some pleural adhesions. The heart was only slightly hypertrophied, and there was a little atheroma of the coronary arteries. The heart-muscle was firm and natural in colour. The endocardium on the left side was white and thick. The valves were natural. So that macroscopic examination failed to reveal anything to account for the very striking symptoms observed during life. The heart was hardened in formalin, and a block of tissue, including the auriculo-ventricular bundle of His, was cut in serial sections by Mr. Shaw, every fifteenth section being mounted. This was the method of examination suggested by Professor Keith, who very kindly examined the sections, and has confirmed my main conclusions. The auriculo-ventricular bundle was found at the level of the node to be composed of badly staining shrunken fibres without striation lying imbedded in fibrous tissue. On tracing the bundle downwards, the same degenerated type of fibres were found in the sections which included the pars membranacea of the septum. Though fibres of the bundle could be made out in the upper and lower parts of the sections at this level, they could not be found in the middle portion, except in the most posterior part of the bundle, where a few fibres were found present. So that almost complete interruption appears to have occurred at this point. At the level of the lower portion of the undefended space the invasion of the bundle by fibrous tissue could be seen very distinctly. At the point where the auriculo-ventricular bundle bifurcates only a few shrunken strands could be seen, surrounded by dense fibrous tissue. From this point onwards there was considerably less evidence of degeneration; a section through the left branch showed some fibrosis around it, but the fibres composing the bundle no longer had the shrunken aspect noted higher up. The longitudinally running fibres of the left branch did not show much alteration. This escape of the fibres below the site of disease has been described by Keith in a case of heart-block of eighteen years' standing.

At the time of this case, 1907, opportunities did not exist for the performance of Wassermann's reaction, but there was nothing in the lesions found to suggest a syphilitic origin, no endarteritis of the vessels in the neighbourhood and no plasma cells.

The bundle was evidently involved in fibrous tissue which was

undergoing contraction, but it is impossible to account for the formation of this fibrous tissue. Out of twenty-seven cases of heart-block coming to necropsy, collected by Thomas Lewis, sclerosis or fibrosis was responsible for six, gumma being the only cause which was more frequent, this occurring eight times. All the other causes given were only responsible for one case each.

Sahli's Hæmoglobinometer.

By A. E. BOYCOTT.

IN order that any form of hæmoglobinometer with a fixed and permanent standard should give correct readings under varying conditions of illumination, it is necessary that the pigments under comparison should be the same—in other words, that the standard should be composed of hæmoglobin, or some derivative of hæmoglobin, and not of red glass or jelly tinted with picrocarmine or some such dye. The two simple instruments in common use which conform to this requirement are the modifications of the Gowers instrument introduced by Haldane and by Sahli respectively. In the former the permanent standard is made by sealing up CO-hæmoglobin in an atmosphere of coal-gas; in the latter it consists of acid hæmatin, and the samples have to be converted into these substances before the comparison is made. In remote places—sometimes, too, in ultra-modern buildings—it may be not a little inconvenient to obtain the carbon monoxide, or coal-gas, which is necessary for the Haldane instrument; the 1 per cent. hydrochloric acid which is required for Sahli's apparatus may, on the other hand, be easily carried about. The pale brown colours which have to be compared in the Sahli instrument are very easy to match, so that at first sight it appears that this apparatus would be the more convenient to use, particularly in cases where the presence of some abnormal pigment in the blood makes the Haldane apparatus difficult or impossible to use.

Some use of Sahli's hæmoglobinometer has, however, shown that it suffers from material inaccuracies. In the first place, the standard does not seem to be adjusted to any definite strength of hæmoglobin, normal blood giving readings varying from 80 to 120 per cent. on the scale with different instruments. The depth of colour of the standard also varies slowly in the direction of becoming weaker; there is, at the

same time, no alteration in the kind of colour to warn one that anything is happening. In the Haldane apparatus the standard solution is always adjusted to the same strength by appropriately diluting blood of which the oxygen capacity has been determined by direct experiment; the standard is usually perfectly permanent and constant, and anything wrong in the solution is at once made obvious by a change in kind of colour from pink towards brown, which cannot fail to attract notice. Now these objections to the Sahli instrument could obviously be got over by standardizing the standard from time to time against a Haldane hæmoglobinometer and correcting the observed figure accordingly. To introduce a satisfactory correction in this way, however, it is necessary that the ratio between the readings obtained by the two instruments should be constant. It appears that this is not the case.

In one series of observations simultaneous measurements were made on a number of experimental animals in duplicate, with two Gowers-Haldane hæmoglobinometers and with a Sahli instrument. A random sample of consecutive observations shows the following result:—

Gowers-Haldane A	B		Sahli		Difference
101	100	...	86	...	-14 per cent.
77	75	...	59	...	-22 "
65	65	...	60	...	-8 "
81	80	...	66	...	-18 "
93	92	...	76	...	-18 "
108	109	...	82	...	-24 "
78	77	...	67	...	-14 "
101	101	...	80	...	-21 "
66	64	...	55	...	-15 "
84	80	...	74	...	-10 "
100	98	...	76	...	-23 "
100	101	...	80	...	-20 "
102	102	...	83	...	-19 "

On the whole, therefore, this particular Sahli instrument gave readings 17 per cent. too low, but the error varies from 8 per cent. to 24 per cent.—a variation which renders accurate work impossible.

If one examines the same sample of blood repeatedly, one cannot rely on obtaining readings which are adequately concordant. Thus the same sample of oxalated blood from an experimental animal was measured five times in parallel with the two instruments, with the following results:—

Gowers-Haldane		Sahli		Difference
125	...	98	...	-22 per cent.
125	...	106	...	-15 "
127	...	85	...	-33 "
129	...	87	...	-33 "
123	...	95	...	-23 "
Average	126	94		25 "

The largest difference with the Gowers-Haldane apparatus was thus 6 points, or 5 per cent.; with the Sahli instrument 21 points, or 22 per cent.

I conclude, therefore, that the Sahli hæmoglobinometer cannot be regarded as an instrument of precision. The explanation of its failure to give concordant readings is probably to be found in the fact that the pigment (acid hæmatin) is not in solution but in suspension. It is easy to see that a 1 per cent. dilution of blood in 1 per cent. hydrochloric acid becomes clearer at the top and darker below if left standing vertically in a test-tube for a few days. This fact is indeed recognized in the more recent forms of the apparatus by the inclusion of a glass bead in the standard solution. When blood is mixed with dilute acid the size of the particles of which the coloured precipitate is composed presumably varies with the precise method of mixture, and the depth of tint seen by transmitted light is thus not always the same when the same quantity of the same blood is mixed with the same quantity of dilute acid. The resultant colour, for example, is not necessarily the same when the blood is put into the bottom of the tube and the acid filled in from above as when the blood is allowed to fall into a tube full of acid. It is obvious that one cannot rely on always making the mixture in precisely the same way.

These considerations naturally suggested that alkaline hæmatin dissolved in alkali would form a more accurate standard, but my own attempts in this direction have been entirely unsuccessful owing to progressive changes in both the depth and kind of colour (possibly due to aggregation) which such solutions undergo. In any case, such a standard would be inconvenient, since one must use either quite strong caustic alkali or heat to effect the conversion of fresh hæmoglobin to alkaline hæmatin within a reasonable time.

An Attempt to differentiate the Diphtheroid Group of Organisms.

By HENRY PRIESTLEY.¹

THE true Klebs-Loeffler bacillus of diphtheria is, in its typical form, a definitely banded slender rod with distinct granulations, and when it occurs in this typical form is usually readily enough recognized by its morphology alone. But this is not the only, nor indeed, perhaps, the commonest form of the diphtheria bacillus. Great variations occur in the length and thickness, the prominence and number of the bands and in the distinctness of the polar granules, and it is occasionally very difficult, if not impossible, to recognize the diphtheria bacillus under these altered morphological conditions. This difficulty is accentuated and made more important by the fact that there is a large group of organisms which more or less closely resemble the diphtheria bacillus, but which do not possess a like significance from the bacteriological or public health point of view. Fortunately these diphtheria-like bacilli have their most frequent habitats in regions other than the throat. This group of diphtheroid or diphtheria-like bacilli thus attains an artificial importance, from the possibility of mistaking its members for the true diphtheria bacillus, quite apart from any pathogenic effect they may have on their own account.

While many examples of the group have been described in the literature, our knowledge of them is in a very unsatisfactory state and no really serious attempt has been made, on the one hand, to classify them among themselves, and, on the other, to furnish some readily applicable test to distinguish them from the true diphtheria bacillus.

The present work was undertaken to determine whether the present bacteriological methods were sufficient to supply such classification and distinction. In the event of these proving unsatisfactory it was hoped that some further methods might be devised to attain these ends, but owing to illness and other causes this part of the work had to be abandoned. It has been deemed advisable, however, to publish the experimental results thus far obtained, although the conclusions reached are largely of a negative character.

¹ From the Lister Institute, London.

BRIEF REVIEW OF THE BIBLIOGRAPHY ON THE DIPHTHEROID ORGANISMS.¹

Diphtheroid organisms—i.e., organisms resembling more or less closely the diphtheria bacillus—have been isolated from almost every part of the human body. They have been found in the nose and throat in normal and pathological states of these parts [1 to 13], in the ear [3, 7, 14 to 27], conjunctiva [3, 28 to 30], urine and urinary tract [31 to 41], the female genital tract [31, 33, 36, 42], in the pus of a liver abscess [43], in empyema [44], in the vegetations of ulcerative endocarditis [45], in the skin in various conditions [24, 30, 31, 46 to 48], in association with leprosy in man [49 to 55], and the so-called rat leprosy [56], and also in the papules of variola and vaccines [30, 57 to 64], and in cellulitis [98]. Much has been made, also, of their occurrence in the cerebrospinal fluid [65 to 68]. Finally they have been observed in milk [31, 60, 69 to 71], in water [72], and in various animals [7, 39, 73, 74]. The most familiar of the diphtheroid organisms is the *Bacillus Hofmanni*, and as it has been described by very many workers, and is generally held to be a definite organism with stable characters, it has not been considered here, and the same is the case with the *Bacillus xerosis*.

Other varieties of diphtheroids have been described in more or less detail by their discoverers, but sufficient data have not been given in most cases to enable one to bring them together into groups, or indeed, in many cases, to say whether an organism has been described before or not. The only attempt which has been made to classify the members of the group from published descriptions is that by Graham Smith [39].

Some writers [18, 20, 78] have laid stress on the association of diphtheroids with the otitis media following scarlet fever, and in the series described below will be found twenty-five strains isolated from cases of scarlatina. Ford Robertson and his co-workers [32, 33, 66, 67] believe that diphtheroids are the causal agents of general paralysis of the insane and of locomotor ataxia, but the consensus of opinion is against this view [75], although some authorities believe that they may have some effect in the production of the terminal symptoms of these diseases [68]. The only other diphtheroids which have been

¹ As the bibliography of the subject is an extensive one, it has been found convenient, for reasons of space, to employ reference numbers in the text instead of authors' names.

claimed definitely as causal agents of disease in man are those found in sore throats by Ruediger and others [4, 5, 6], the *Bacillus coryzae segmentosus* in "colds" [76], and the acne bacillus of Sabouraud.

In other cases the association of diphtheroids with morbid conditions has not usually been strongly insisted upon and their importance for human pathology has not been considered great.

SOURCE OF STRAINS EXAMINED IN THE PRESENT RESEARCH.

For this investigation diphtheroids were obtained from the mouth, nose, eye, ear, urine, urethra, vagina, and vulva, pus from tuberculous abscess of the hip, the skin in leprosy, and a few from unknown sources. Forty-nine strains in all were examined, of which twenty-five came from ears and the results are tabulated in the accompanying table. The preponderance of strains from ears was intentional.

It was hoped that some definite type might be found around which to group the remaining types. Moreover, many authorities [17, 19, 21, 22, 77] have described the occurrence of diphtheria bacilli in the ears of scarlet fever patients usually after very imperfect examinations, and it was hoped that this matter might be cleared up. Further, several authorities [18, 20, 78] have regarded the otitis media following scarlet fever as due to the presence of diphtheroids, and it was therefore thought that some additional light might be thrown on this question. On this last point, however, no conclusions were arrived at.

Strains from Otitis Media following Scarlatina.

Although sixty-nine cases of scarlatina were examined, and I am very much indebted to Dr. Thompson, of the North-Eastern Fever Hospital, for material, only four of these had otitis media. From three of these four cases strains of diphtheroids were isolated. These were identical in all the characters investigated (*see* Table S5) and correspond to no other strain isolated. It may be remarked that all three cases were in the same hospital at the same time, so that this fact, with the small number of observations, precludes the possibility of any conclusions being drawn. From the fourth case no diphtheroid was isolated.

Strains from the Ear.

In the examination of the ears the procedure was in all cases the same. Swabs were taken in the usual way, and cultures made on solidified serum. After twenty-four hours' incubation, and, again, after a further twenty-four hours' incubation, the growth, if any, was examined, and if diphtheroids were observed in smears stained with Loeffler's methylene blue, plates were made with serum agar, and the diphtheroids isolated where possible. The ears of eighteen normal persons were examined in this way, and in fifteen of them diphtheroids were observed. Of these, eight were isolated and examined in detail (*see* Table, E). These eight strains were identical, and the remaining seven, which were not isolated in the pure state, were morphologically, to all appearances, the same organism. They correspond in all details, so far as data are available, with the diphtheroid *Bacillus ceruminis* isolated by Graham Smith [7] from normal ears.

It seems reasonable to infer, therefore, that this is the type most commonly met with in normal ears, and hence its finding in pathological states must be considered to have less significance than it might otherwise have.

Strains from the Ear in Scarlatina.

From the sixty-nine cases of scarlet fever diphtheroids were obtained in thirty-two. Of these, twenty-five were isolated and examined in more or less detail. They showed, however, little uniformity, and fall into as many as nine groups. One group corresponds to the strain met with in normal ears, and consists of only two members. Another group (S5) of three members was found in the otitis cases. The largest group (S13) is represented by four members, and another strain closely resembling, or identical with, *Bacillus Hofmanni* contains three members (S1). No other strain consists of more than two members, and the majority contain only one.

Hence it appears that there is no special type of diphtheroid occurring in the ears in scarlatina, and they are not more common than in normal ears. Of course, the differentiation depends on the value which can be placed on the methods used, of which more will be said later; but some of them differ very markedly from one another—e.g., S13 and S38. A similar lack of uniformity was found in strains examined from other sources than ears.

Strains from other Sources.

I am indebted to Dr. Eyre, of Guy's Hospital, for many cultures from various sources containing diphtheroids, and to Dr. Arkwright and Dr. Bayon for pure cultures of C16 and B respectively. The remaining material was obtained from the Diagnosis Department of the Lister Institute.

The sixteen strains from sources other than ears fall into thirteen groups, most of which consist of only one member. One group isolated from urethral pus in cases of gonorrhœa consists of three members.

Hence it appears that the diphtheroids which are met with in various parts of the body form a very large series which cannot be arranged in groups, and vary as much among themselves as the equally ubiquitous streptococci.

The differentiation of the diphtheroids, as a whole, from the true Klebs-Loeffler bacillus is usually easy enough, if one takes into consideration all the cultural and morphological characteristics. There is no one character, however, which can be looked upon as reliable.

As we have seen, in the case of some strains of diphtheroids, the morphology is of little assistance. The fermentation reactions do not afford a much more reliable guide, except as regards *Bacillus Hofmanni*. These have been investigated to some extent by several workers [79 to 83].

The usually accepted fermentation reactions of the *Bacillus diphtheriæ* have been placed in the table for convenience of reference. It will be seen that in several cases the fermentation reactions of several diphtheroids (S19, G13, G5), which were undoubtedly not *Bacillus diphtheriæ*, approximate very closely to those of *Bacillus diphtheriæ*, especially when one considers that the acid production from saccharose and lactose is not usual in *Bacillus diphtheriæ*, and from glycerine and dextrine, is not invariable.

The formation of acid from dextrose has been frequently looked upon as being considerably in favour of an organism being *Bacillus diphtheriæ*; but it will be seen from the table that it has proved unreliable in differentiating the strains I have examined. Of the eighteen strains tested, fifteen produced acid from this sugar, and six of them (G13, C16, G12, D1, X, and S5) within twenty-four hours.

Myer Coplans [92, 93] makes use of a medium consisting of serum, glucose, neutral red, CaCl_2 and KCNS. "Colonies of diphtheria

appear almost invariably to yield a bluish-pink tint with diffusion of like tint through the medium; but with *Bacillus Hofmanni* the growth is yellowish and alkaline." This medium was tried in several cases, and found to be quite satisfactory in distinguishing between a typical acid-producing diphtheria bacillus and a non-acid-producing bacillus like *Bacillus Hofmanni*. Goodman [94] and Clark [95], however, have shown that different strains of the diphtheria bacillus vary considerably in acid production from glucose, from almost nothing up to a large amount: so that for the low acid producers this medium would not be satisfactory. Then, too, it will not serve to distinguish between the diphtheria bacillus and acid-producing diphtheroids.

PATHOGENICITY EXPERIMENTS.

None of the strains tested was found to kill a guinea-pig of 250 gm. when 2.5 c.c. of a forty-eight-hour broth culture was injected under the skin of the abdomen.

The usual method of injecting a given quantity of a twenty-four or forty-eight-hour broth culture into a guinea-pig is not satisfactory for comparative purposes, as even in the case of two strains of the same organism—say *Bacillus diphtheriae*—1 c.c. of one culture may contain many millions more organisms than 1 c.c. of another culture.

Experiments with the object of devising a more satisfactory method of giving more uniform doses were in progress, but had to be abandoned. Arkwright¹ has recently recorded experimental results dealing with the variations in virulence of *Bacillus diphtheriae*.

SEROLOGICAL TESTS.

Immunity reactions have been used by various authorities in the hope of differentiating the *Bacillus diphtheriae* from some of the diphtheroids [84 to 89]. These were investigated to some extent, and found to be unsatisfactory.

AGGLUTINATION EXPERIMENTS.

A rabbit was immunized against *Bacillus diphtheriae* by nine injections, first of killed bacilli, and later of living bacilli up to two agar slopes of living virulent bacilli. The serum from this animal was found

¹ Journ. of Hyg., xi, p. 409.

to agglutinate the homologous strain completely in a dilution of 1—1,600, and had no effect on *Bacillus Hofmanni* and the diphtheroid tested (D1)

The great majority of genuine diphtheria strains tested (twelve out of fifteen strains) agglutinated spontaneously, however, so that the method cannot be considered a practicable one. Various means were tried to prevent this spontaneous agglutination, such as the addition of glycerine, formalin, various salts, &c., but with no success.

The agglutination of the homologous strain, moreover, presented some curious features. There was little or no agglutination after three hours at 37° C., and it was not marked until a further period of twenty-four hours had elapsed at room temperature, after which it proceeded rapidly and was almost complete at 1—1,600 in a few hours, the controls remaining throughout free from agglutination. It was found that the use of a solution containing 1 per cent. of KCl and 0.25 per cent. of CaCl₂ instead of normal saline solution, for dilution purposes, accelerated the action markedly, for there was distinct agglutination in six hours. Moreover, this solution increased the action, for agglutination was complete at 1—6,400 instead of 1—1,600, the controls remaining unchanged.

PRECIPITATION EXPERIMENTS.

Precipitation experiments were also tried with this serum, using as antigen an extract prepared from bacilli by Dean's method [90].

A precipitate at 1—20 was obtained with the homologous bacillus, but not with several other strains of *Bacillus diphtheriæ* tested. Later on an extract was prepared by Rowland's method [91] and gave a precipitate at 1—32, but this could not be followed up.

COMPLEMENT FIXATION TESTS.

These gave absolutely no results, probably owing to the want of a satisfactory antigen.

Bacterial extracts prepared by Dean's methods, and bacterial solutions in weak antiformin, were used without success. It will be seen that the immunity reactions examined were without exception unsatisfactory, and a further investigation seemed necessary before applying any of the reactions to the diphtheroid organisms, but illness prevented the carrying out of this.

VIRULENCE TESTS.

The most useful of all the ordinary laboratory methods for distinguishing true diphtheria bacilli from bacilli resembling them is the virulence test. This, however, does not serve to distinguish between avirulent diphtheria bacilli and avirulent diphtheroids. Several authors [4, 5, 6] have described diphtheroid organisms which are virulent and kill laboratory animals, but the animals are not protected by diphtheria antitoxins.

The cultural characteristics of the diphtheria bacillus on serum and other media are much too variable to be of great use in the differentiation of the true diphtheria bacillus from diphtheroids. For each medium, however, there is a form of colony which the diphtheria bacillus most commonly presents.

On examination of the table it will be seen that several of the diphtheroids investigated presented growths very much resembling the typical growths of the diphtheria bacillus. It should be added that the cultures were grown on serum, agar, and broth for twenty-four hours at 37° C., unless otherwise stated. The fermentation reactions given in the table were observed in Hiss's serum water medium [96], kept for ten days to a fortnight at 37° C. The production of acid was in all cases, however, evident within the first forty-eight hours.

In describing the morphology of the diphtheroid organisms use has been made of the classification of Westbrook, Wilson, and McDaniel [97], for it is more convenient and more exact than the usual morphological descriptions.

It is obvious that the results obtained are all of a negative character, and go to show that there is no one reliable method at present in use which will in all cases without exception distinguish the true diphtheria bacillus from diphtheria-like bacilli other than *Bacillus Hofmanni*. Further, the present bacteriological methods are not sufficient to give a basis of classification of the diphtheroid organisms among themselves. The diphtheroid organisms have been shown to be almost as ubiquitous as the streptococci, and to present as great difficulties in their differentiation and classification.

	Source	Morphology	Gram	Neisser	Growth on serum	Growth on agar	Growth on gelatine
	— Throat in diphtheria	Diphtheria bacillus	+	+
G13	In pus from T.B. abscess of hip	On serum banded and mostly of D1 type; on agar show single median septum	+	—	Greyish-white growth of small, circular, discrete colonies	Thick growth of raised, circular, discrete, greyish-white colonies	Good growth in 5 days of raised, circular, white colonies
S19	Ear in scarlet fever	Short banded bacillus of E1 type; very well-marked polar granules	+	+	Minute, circular, raised, discrete, white colonies, like K.L., but smaller	Greyish, film-like growth of minute, circular, flat colonies	No growth
G5	Urine in T.B. cystitis	Short, slender, banded bacillus, mostly of E1 type	+	+	Cream-coloured, dry, minute, circular colonies; very adherent to medium	Minute, raised, white colonies with ground-glass surface	Very slow growth of minute colonies
C16	Throat in diphtheria	Mostly solid staining or of D2 type	+	—	Pure yellow, thick, confluent growth	Yellow colonies with crenated edges	Pale yellow, raised colonies in 30 hours
G8	Urethral pus (3 strains)	Irregular, curved banded bacilli of A1 and C1 types; many clubbed	+	+	Minute, white colonies like K.L., but smaller	Very minute, greyish-white, circular colonies	No growth
G6	Urine in T.B. cystitis	Short, oval bacillus with single, unstained septum; some banded and clubbed; arrangement marked	+	+	Very like diphtheria bacillus	Good white growth, like diphtheria	No growth
S13	Ear in scarlet fever (4 strains)	Long, narrow, clubbed and curved bacilli, banded and of A1 type	+	—	Small, raised, white, circular colonies, like K.L.	Film-like growth of very minute, greyish, circular colonies	No growth
G12	Vagina in vaginitis	Small, plump, oval bacilli of D2 type, with single median septum; later most are banded and of D1 type	+	+ Very scanty granules	Small white colonies, like K.L.	White colonies, like K.L.	Like K.L. in 36 hours
D1	Throat in diphtheria (2 strains)	Very like <i>Bacillus Hofmanni</i> of D2 type	+	—	Pure yellow, raised, circular colonies, like K.L., except in colour	Like K.L., but pure yellow	Discrete small colonies, yellow

Growth in broth	Growth on potato	Dextrose	Lavulose	Saccharose	Lactose	Maltose	Mannite	Dulcite	Glycerine	Dextrine	Galactose	Milk	Virulence
...	...	+	+	⊕	⊕	+	-	-	+	+	+	+	+
Turbid growth, with deposit	...	+	+	+	-	+	-	-	-	-	+	-	Non-virulent
Turbid, with slight deposit	...	+	+	+	+	+	-	-	+	+	+
Turbid growth	...	+	+	-	+	+	-	-	-	-	+	-	Non-virulent
Slight turbidity and pellicle	Slight colourless growth	+	+	+	-	+	-	-	-	-	-	Alk.	Non-virulent
No growth	...	+	+	-	-	-	-	-	-	-	-	Alk.	...
...	...	+	+	+	-	+	-	-	-	-	-	-	...
Broth clear, with slight granular deposit	...	+	+	-	-	+	-	-	-	-	-	-	...
Turbid, with deposit	...	+	+	-	-	+	-	-	-	-	-
Broth clear, with deposit	Almost invisible, colourless growth	+	+	-	-	+	-	-	-	-	-	-	Non-virulent

	Source	Morphology	Gram	Neisser	Growth on serum	Growth on agar	Growth on gelatine
X	Not known	Short, slender bacilli, with single median septum; few banded	+	+	Growth like K.L.	Thick, greyish-white growth of circular colonies	...
S79	Ear in scarlet fever	Short, thick bacilli of D2 type; few banded forms	+	-	Growth like K.L.	Raised, white, circular colonies	...
S5	Ear in scarlatinal otitis media (3 strains)	Long, slender, banded and clubbed of A1 and C1 types	+	+	Thick, confluent, moist, pink growth	Large, circular, raised, pink colonies	No growth
G16	Vagina in vulvitis	Medium-sized banded and clubbed bacilli, mostly of D1 type	+	+	Very minute greyish-white circular colonies	No growth in 24 hours; later, very minute greyish, circular colonies, with filmy edges	No growth
G4	Eye in hordeolum	Medium length, fairly thick, most of D2 type, some banded	+	+	Raised, circular, discrete colonies like K.L., but smaller	No growth in 24 hours; later, very minute greyish-white, circular colonies	Very minute colonies after some days
B	Skin in leprosy	Very irregular, bacilli mostly of A type; clubbing very marked, also polar granules	+	+	Raised, white, circular colonies, like K.L.	Very minute, circular, greyish-white colonies	...
S1	Ear in scarlet fever (3 strains)	Nearly all of D2 type; few banded forms (<i>Bacillus Hoffmanni</i>)	+	-	Raised, circular, white colonies like K.L.	Raised, white, circular colonies 1 mm.	...
E	Normal ears and ears in scarlet fever (10 strains)	Medium length, slender bacilli, solid staining, with well-marked polar granules, some with one or several septa (<i>Bacillus ceruminis</i>)	+	+	Growth very like K.L.	Minute creamy-white colonies	No growth
S38	Ear in scarlet fever	Long, slender, banded bacilli, marked terminal granules	+	+	Like K.L.	Thick, white, waxy-looking growth	...
S42	Nose in scarlet fever	Short, thick bacilli, some banded, others with single septum	+	+	Very faint, white growth	No growth in 24 hours; later, very minute circular colonies	...

	Source	Morphology	Gram	Neisser	Growth on serum	Growth on agar	Growth on gelatine
S58	Ear in scarlet fever	In 48 hours on serum; medium length, slender, curved bacilli, with very numerous granules	+	+	Very minute white colonies	No growth in 24 hours; later, very minute colonies	...
S95	Ear in scarlet fever (2 strains)	Slender bacilli, mostly solid staining; few banded, well-marked polar granules	+	+	Creamy-white confluent growth	Large, circular, white colonies	...
G:20	Unknown	Mostly clubbed bacilli of A and A1 types; very prominent polar granules	+	+	Creamy-white circular colonies	Filmy growth of minute, circular colonies	...

CONCLUSIONS.

(1) Forty-nine strains of diphtheroids have been obtained from various parts of the human body, and examined by the usual bacteriological methods.

(2) Thirty-three of these strains were isolated from the external auditory meatus, eight from normal persons and twenty-five from persons suffering from scarlatina.

(3) It was found that there was no definite type of diphtheroid organisms peculiar to the ears of scarlatina patients. There is, however, apparently a definite type of diphtheroid occurring in the ears of normal persons.

(4) The fermentation reactions were not found to be a very satisfactory method for the separation of the different strains of diphtheroids included in this research from one another, and from the true *Bacillus diphtheria*. In particular the fermentation of glucose is of little value.

(5) Serological tests were without exception unsatisfactory.

(6) For the differentiation of the diphtheroid organisms from one another, and from the true *Bacillus diphtheria*, all the cultural characteristics must be considered.

In conclusion, I wish to thank Dr. Eyre, Dr. Thompson, Dr. Arkwright, and Dr. Bayon for material, and Dr. Henderson Smith for the assistance he has given me during the course of the investigation.

Growth in broth	Growth on potato	Dextrose	Lactulose	Saccharose	Lactose	Maltose	Mannite	Dulcitol	Glycerine	Dextrine	Galactose	Milk	Virulence
No growth
Slight turbid- ity, with de- posit
...

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The Relation between the Fixation of Complement and the Formation of a Precipitate.

By H. R. DEAN.¹

ONE of the most interesting problems connected with immunity is the explanation of the process by which complement is absorbed by the mixture of an antigen with its homologous antibody.

One theory explains the phenomenon by assuming the existence of an amboceptor or interbody with two affinities, the one of which unites with the cell to be dissolved, while the other unites with the complement. According to the other view the complement is taken up by the complex formed by the union of cell and antibody, the antibody being supposed to act somewhat after the manner of a mordant.

The fixation of complement experiments of Bordet and Gengou have naturally received two different explanations. According to the one view the complement is fixed by the precipitate which is formed by the union of antigen and antibody. According to the other view, precipitation and complement fixation are two entirely separate and independent phenomena. The fixation of complement is attributed to the action of an amboceptor, and some workers have gone so far as to state that a special variety—"a complement-fixing amboceptor"—exists. This amboceptor, which they call a *Bordet amboceptor*, is considered to be distinct from the amboceptor concerned in bacteriolysis.

The controversy which arose between the supporters of these two explanations resulted in the publication of a large number of papers. Only the more important of these communications are here summarized.

In 1901, Bordet and Gengou showed that alexin was fixed by the mixture of a bacillary emulsion with its homologous antiserum. In the same year, Widal and Le Sourd (1901) confirmed this result, and succeeded in demonstrating that the serum of typhoid fever patients would bind complement in the presence of an emulsion of *Bacillus typhosus*. In 1902, Gengou extended the scope of the reaction by showing that the serum of animals which had been injected with a foreign proteid had acquired the property of fixing complement if mixed

¹ From the Bacteriological Laboratory, Lister Institute. The first part of this paper was read at the meeting held on March 21.

with that proteid. Despite the importance of this discovery, however, the next two years were not productive of any substantial addition to the literature of the subject. Interest in the question appears to have been revived by Moreschi (1905), who pointed out that the results which had been attributed to the action of anti-complements were in reality due to the fixation of complement by a mixture of antiserum with its homologous proteid. In the same year (1905), Neisser and Sachs applied the principles laid down by Moreschi to the production of a practical method for the identification of the blood of different animals. In subsequent papers Moreschi (1906) and Moreschi and Pfeiffer (1906) advanced the view that the complement was taken up by the precipitate. Moreschi concluded that precipitin and precipitinogen unite in variable proportions, and form a series of precipitates, which possess a more or less strong anti-complementary action. About the same time, and independently of Moreschi, the same explanation was put forward by Gay (1905), who came to the conclusion that the precipitate fixed the complement. In support of a criticism of the views of Neisser and Wechsberg (1901), it was shown by Gay (1905) that the amount of interference with hæmolysis was in proportion to the amount of precipitate formed, and this to the amount of antiserum present. Klein (1905) found the fixation of complement closely associated with the formation of a precipitate, and took up essentially the same position as Moreschi and Gay.

On the other hand, Neisser and Sachs (1906) found that the amount of precipitate and the capacity for binding complement stood in no direct proportions. They were able to obtain marked fixation of complement when no precipitate could be recognized. They attributed the fixation of complement to a union of the complement with the complementophile group of an amboceptor, in strict accordance with the theory of Ehrlich. The question has been critically reviewed by Muir and Martin (1906), who added the results of their experiments on the subject. Muir and Martin found that the fixation of complement was as a rule closely associated with the formation of a precipitate, but were not convinced that precipitation formed a complete explanation of complement fixation. They cited as an instance a rabbit v. guinea-pig serum which produced, when mixed with its homologous antigen, a faint cloudiness, but no definite precipitate. The capacity for fixing complement, however, was possessed by this serum to a very high degree. In other experiments they found that, if the antigen was greatly diluted, no precipitate was formed, but the mixture was able

to bind complement efficiently. They also observed during the process of immunizing a rabbit with human serum that the complement-binding properties of the antiserum could be demonstrated at an earlier date than the precipitating properties. Similar results were obtained by Altmann (1910), who immunized a series of rabbits with *Bacillus paratyphosus* B. In many cases it was found that the serum of these animals developed complement-binding properties before they could be shown to have developed agglutinating properties. In the case of one rabbit only, the agglutinating property was the first to appear. After a second injection it was found that the complement-fixing property of the serum was lost during the two days immediately following, while the agglutinating property during the same period showed only a reduction. When rabbits were injected with *Bacillus typhosus*, it was found that the development of the two properties ran a fairly parallel course, though there was some tendency for the agglutinating property to appear earlier than the complement-fixing property. When *Bacillus coli* was used for immunization, the authors found that the power to fix complement appeared earlier in the case of nine rabbits, but in the case of two rabbits marked agglutinating power developed, but little or no power to fix complement. Altmann concluded that the discrepancy was due to differences in the individual strains of bacteria. He considered that certain strains of *Bacillus coli* tended to induce the production of agglutinins, while others tended to produce complement-binding antibodies. Altmann regards these experiments as evidence that the agglutinins are distinct from the antibodies which are responsible for complement fixation.

Wassermann and Bruck (1905), who also consider that complement fixation is due to amboceptor action, adopted a different method with the object of supporting their view. A bacterial extract was prepared, which, when mixed with its homologous antiserum, produced a precipitate, and also a fixation of complement. This extract was set aside, and, after the lapse of some time, was found to have lost its power of producing a precipitate without any loss of its complement-binding properties. This experiment is quoted by Sachs and Altmann (1909) as conclusive proof of the separate identity of precipitins and complement-binding amboceptors.

Evidence of a similar nature was obtained by Friedberger (1906). This observer heated an antiserum, obtained by injecting a rabbit with sheep serum, for one hour at a temperature of 67° C. This heated serum was found to have lost the property of forming a precipitate, while the property of fixing complement had been retained.

By injecting a rabbit with human serum, Friedberger obtained an antiserum so powerful that complement fixation could be obtained by the use of extraordinarily small quantities of the antigen (human serum 1 in 1,000,000,000). When these extraordinarily small amounts of antigen were used no trace of a precipitate could be detected, complement was nevertheless efficiently fixed.

Liefmann (1906) published a series of experiments, the general object of which was to obtain conditions under which complement fixation occurred without the formation of a precipitate. In the majority of his experiments he found that the two reactions were closely associated. He found, however, that if a serum (antigen) was heated, it lost its property of forming a precipitate when mixed with the homologous antiserum. Nevertheless, a mixture of the heated serum with the antiserum produced a marked fixation of complement. Liefmann concluded that the data at his disposal were insufficient to permit of a definite opinion being formed.

In a subsequent paper, Moreschi (1906) appears to have obtained results which are at variance with his earlier experiments. He prepared antisera by injecting hens and ducks. The antisera so obtained gave good precipitates, but bound no complement.

Other instances of precipitation without complement fixation have been recorded by Sobernheim (1906), who experimented with anti-tuberculous sera, obtained by the injection of tubercle bacilli and tuberculin.

For a complete review of the subject, as well as for further references to its literature, the reader is referred to the articles on complement fixation by Meier (1909) and Sachs and Altmann (1909).

The above summary shows that the opinion of the majority, and perhaps the bulk of the evidence, is in favour of the view that the complement-binding bodies are distinct from the precipitins. The evidence for the separate identity of precipitins and complement-binding amboceptors falls under four headings:—

- (1) Complement fixation can be demonstrated in mixtures which contain so small a quantity of antigen that no precipitate can be detected.

- (2) Certain antisera have been observed to give a precipitate, with little or no complement fixation.

Other antisera have good complement-binding properties, but form little or no precipitate.

- (3) If either the antiserum or the normal serum (antigen) is heated

the property of forming a precipitate is lost, but the property of fixing complement remains. If a bacterial extract is kept for a time it loses its property of forming a precipitate with the homologous antiserum, but retains the property of fixing complement.

(4) During the process of immunization the complement-fixing property has been found to appear before the property of forming a precipitate.

OBJECT OF THE EXPERIMENTS.

The general object of these experiments has been to determine whether any relationship exists between the amount of precipitate formed and the amount of complement fixed. Before describing the experiments it seems advisable to refer briefly to the experiments of Chapman and Welsh. The papers which have been quoted were written at a time when it was generally assumed that the antiserum, the so-called precipitin, precipitated the antigen, the so-called precipitinogen. It was, in fact, generally held that the precipitate was derived from the antigen. Chapman and Welsh (1906-11) have, however, shown by numerous and exact experiments that the precipitate is almost, if not entirely, derived from the antiserum. It is the antiserum, in other words, which is precipitated by the antigen. It follows, then, that the amount of the precipitate is proportional to the amount of antiserum present. If, then, the formation of a precipitate is the cause of the fixation of complement, it becomes necessary to show that the amount of complement fixed is proportional to the amount of antiserum present. As already stated, Gay arrived at this conclusion in his explanation of the deviation effects produced by excess of antiserum in hæmolysis. It is not, however, an easy matter to show that this relationship exists, for, as will be seen later, the amount of the precipitate is not the only factor which determines the amount of complement fixed.

It is necessary to refer to one other point in connexion with precipitation. Chapman and Welsh found that a considerable time (up to ninety-six hours) was necessary for the complete precipitation of a given quantity of antiserum. In a complement fixation experiment it is obviously necessary to allow only a short time (about one hour) for the reaction. In the experiments to be described it was desired to compare the amount of complement fixed with the amount of precipitate formed. To do so it became necessary to estimate the amount of precipitate formed during the time allowed for the fixation

of complement. The figures given in the tables represent the precipitate formed in a given time, and do not necessarily represent the entire precipitable content of the amount of antiserum employed.

THE METHOD OF THE PREPARATION OF ANTISERA AND OTHER MATERIAL USED IN THE EXPERIMENTS.

Very little need be said as to the preparation of the antisera, which were all obtained from rabbits which had been immunized, either by the intravenous or the intraperitoneal method. Intravenous injection was used in nearly every case, and in most cases some four to six injections were given at intervals of four days. The sera were inactivated before use by heating for half an hour at 56° C. The antigens employed were: egg-white, horse serum, goat serum, human serum, monkey serum, and emulsions in normal saline solution of a twenty-four-hours' agar culture of *Bacillus typhosus*. The bacterial extracts used in some of the experiments were prepared by a method described in the *Proceedings of the Royal Society of Medicine* (Pathological Section), 1911, vol. iv, No. 6, p. 251.

The red corpuscles used in the complement fixation experiments were obtained by defibrinating the blood of a sheep, and then washing the corpuscles in three changes of saline solution. The hæmolytic serum was inactivated by heating it for half an hour at a temperature of 56° C. Fresh guinea-pig serum obtained from an animal killed on the day of the experiment was used as complement.

DESCRIPTION OF EXPERIMENTS AND RESULTS.

In the majority of these experiments the following method was employed: A series of progressive dilutions of the antigen was prepared in such a way that each successive tube contained half the amount of antigen contained in the tube immediately preceding it in the series. To every tube was then added a constant quantity of the antiserum. As a rule four such sets of tubes were prepared. One of these sets was set aside, that the appearance and amount of the precipitate in each tube might be observed and recorded. To the other sets was added complement in three different quantities or doses and, after one hour's incubation, a sufficient quantity of sheep corpuscles and hæmolytic serum. The set, to which no complement was added, provided a series of precipitates which varied not only in actual amount, but also in the rate of formation and in the size of their constituent

particles. The other three sets of tubes provided a roughly quantitative measure of the amount of complement bound by the various precipitates produced.

The progress of events in the tubes set aside for precipitation was as follows: Immediately after antigen and antibody had been mixed, a distinct turbidity was visible in two or three of the tubes of the series. The tubes which showed an instantaneous change were those tubes which contained antigen and antibody, in the proportions most favourable to the formation of precipitate. After five or ten minutes, or even sooner, very small particles became visible in the tubes which had been the first to become turbid. Below what may be termed the zone of optimal precipitation, that is to say, in the tubes which contained less than the optimal amount of antigen, turbidity in various degrees gave place gradually and progressively, tube by tube, to a condition in which the individual particles become visible to the naked eye. The particles in the tubes of the zone of maximal precipitation rapidly increased in size, and at the end of some twenty minutes it was usual to find that in two or three tubes large flocculi had separated, which rapidly fell to the bottom of the tube, leaving a perfectly clear supernatant fluid.

In such a series of tubes it was possible to recognize three zones: (1) A zone where the proportion of antigen to antibody was such as to produce rapid and complete precipitation. It may be assumed that in these tubes the antigen was able to rapidly precipitate the precipitable substance of the antiserum. (2) A zone in which the antibody was present in relative excess. In these tubes turbidity made its appearance slowly, and uniform turbidity slowly gave place to a condition in which small particles could be distinguished. In tubes in which a great excess of antibody was present the appearance of turbidity was still further delayed and, during the time of the experiment, the precipitation process did not go beyond the formation of an apparently homogeneous turbidity. (3) A zone where the antigen was present in relative excess. In these tubes the process of precipitation was slow. Turbidity appeared only after a considerable interval, and the appearance of separate particles was often delayed for some hours. A great excess of antigen entirely inhibited the formation of a precipitate.

Relative excess either of antigen or antibody was found to slow the process of precipitation, and if the excess was at all considerable, to lessen the amount of the precipitate.

The result of a typical experiment is given in Table I.

DESCRIPTION OF EXPERIMENT I AND NOTES ON THE COURSE OF THE REACTION.

Column A represents the results of the precipitin experiment. Columns B, C, and D represent the results of the complement fixation experiments.

The tubes 1 to 11 in column A contained a bulk of 10 c.c., made up of 5 c.c. of the diluted goat serum (antigen) and 5 c.c. of a 1 in 10 dilution of rabbit and goat serum (antibody). The lower portion of each of these tubes was narrow and calibrated. The tubes were incubated for four hours at 37° C. and the progress of the precipitation was observed and recorded at regular intervals. *Immediately after mixing* turbidity appeared in tubes 2 and 3.

At the expiration of ten minutes flocculi were apparent in tubes 2 and 3, and tubes 1, 4, and 5 showed uniform turbidity. *After half an hour* large flocculi, which had formed in tubes 2, 3, and 4, had fallen to the bottom of the tubes and left a clear supernatant fluid. Flocculi had formed in tube 1, but had separated less completely. Small particles were visible in tube 5 and just visible in tube 6. In tubes 7 and 8 turbidity was present without visible particles. *After one hour* the first six tubes showed a deposit and a clear supernatant fluid. Tube 7 showed small particles suspended uniformly throughout its contents. In tubes 8, 9, and 10 a progressively diminishing opalescence was seen. *After four hours* all the tubes were centrifugalized and the actual amount of the deposited precipitate was read. The figures are recorded in column A.

In order to save unnecessary complexity the necessary control tubes have been omitted from the table. Control tubes containing the various dilutions of antigen without antiserum, and a tube containing a 1 in 10 dilution of the antiserum without antigen, were incubated for the same period (four hours) and remained absolutely clear.

The tubes in columns B, C, and D received each 0.5 c.c. of the various dilutions of goat serum (antigen) shown in the table. To all the tubes were then added 0.5 c.c. of a 1 in 10 dilution of antiserum and 0.5 c.c. of diluted guinea-pig complement. The tubes in column B received 0.05 c.c. guinea-pig serum diluted to 0.5 c.c., in column C 0.1 c.c. guinea-pig serum diluted to 0.5 c.c., and in column D 0.2 c.c. guinea-pig serum diluted to 0.5 c.c. All the tubes were then incubated for one hour at 37° C. in the same incubator as the tubes prepared

for the precipitin reaction. Both the precipitin and the complement fixation experiments were carried out with the same materials and as nearly as possible at the same time and under the same conditions. After one hour's incubation all the tubes received 0.5 c.c. of a 1 in 20 suspension of washed sheep corpuscles and 0.5 c.c. of a 1 in 500 dilution of hæmolyisin (rabbit v. sheep). The tubes were then incubated for one hour, at the end of which time the results were read and recorded.

The fresh guinea-pig serum (complement) was separately titrated and its value determined; 0.02 of this serum diluted to 0.5 c.c. and added to 0.5 c.c. of a 1 in 500 dilution of hæmolyisin, 0.5 c.c. of a 1 in 20 suspension of sheep cells and 1 c.c. of normal saline solution produced complete hæmolysis after one hour at 37° C. This was the smallest quantity of complement which produced complete hæmolytic action in conjunction with 0.5 c.c. of a 1 in 500 dilution (two hæmolytic doses) of the hæmolytic serum. If we accept 0.02 c.c. as one lytic dose of the complement, column B represents the fixation of two and a half minimal lytic doses of complement, column C five minimal lytic doses, and column D ten minimal lytic doses. In the case of tube 6 of column D, nearly ten doses of complement were fixed.








A titration of the antiserum (rabbit v. goat) established the fact that this serum had a strong hæmolytic action on sheep corpuscles. This explains the fact that in this experiment complement fixation was not a more delicate indicator of the presence of a trace of antigen than the precipitin reaction.

It appears from this experiment that using a 1 in 10 dilution of antiserum the largest precipitate was obtained by adding an equal quantity of a 1 in 10 dilution of antigen. The greatest fixation of complement was obtained by adding to a 1 in 10 dilution of antiserum an equal quantity of a 1 in 320 dilution of antigen.

Remarks on Table I.

From a consideration of Table I it is evident that the proportions of antigen and antibody which produce the largest quantity of precipitate are not those which affect the greatest fixation of complement. In this case a mixture of a 1 in 10 dilution of antigen with a 1 in 10 dilution of antiserum produced a large precipitate, but did not fix two and a half minimal lytic doses of complement. Similar and consistent results were obtained by mixing a variety of antigens with the homologous antisera. It was determined that mixtures which

rapidly produced a large flocculent precipitate had little or no power to bind complement. If, however, the relative properties of antigen and antibody were such that the precipitate formed slowly, the mixture was found to have very distinct power to bind complement. Roughly speaking, the maximal fixation of complement corresponded to the mixture of antigen and antibody which at the expiration of half an hour showed the greatest uniform turbidity. If to a series of dilutions of the antigen was added a constant amount of antibody, two tubes

No Hæmolysis	
Trace "	
Slight "	
Half-Hæmolysed	
Strong or Marked Hæmolysis	
Almost Complete Hæmolysis	
Complete Hæmolysis	

Explanation of Scheme used to illustrate the Complement Fixation Experiments.

Each tube in the original experiment is represented by a square in the table. A black square represents total hæmolysis or no fixation of complement. A white square represents a tube in which no hæmolysis has occurred, that is to say, a tube in which all the complement has been fixed.

could be picked out from the set—the one contained the proportions of antigen and antibody which produced the largest precipitate, the other the proportions of antigen and antibody most favourable to complement fixation. With constant antibody the amount of antigen necessary to produce the maximal fixation of complement was much smaller than the amount of antigen necessary to produce the largest amount of precipitate. In the experiment recorded in Table I it was found that thirty times as much antigen was required to produce the maximal precipitate as was necessary to produce the maximal fixation of complement.


































The process which causes both precipitation and complement fixation is in all probability the aggregation of molecules present in the antiserum by the action of the antigen. When sufficient antigen is present aggregation takes place energetically and large flocculi are rapidly separated. These are the conditions favourable to the precipitation reaction. If a relatively smaller amount of antigen is present, the process of aggregation is slower and less complete. These are the conditions favourable to complement fixation. Under these conditions the individual particles which form the precipitate are extremely small, but the surface afforded by all the particles of such a precipitate must be much larger than that offered by a precipitate composed of large flocculi. It is indeed possible that there is a direct relationship between the surface area of the particles of the precipitate and the amount of complement absorbed.

In any case it is probable, for reasons that will appear from an experiment to be described later (Table II), that complement is fixed during the earliest stages of the formation of the precipitate, and that consequently the proportions of antigen and antibody which cause a very slow precipitation are those favourable to the fixation of complement. The fixation of complement seems to stand in close relationship with the rate of formation and the state of division of the precipitate. It can, in fact, be shown experimentally that either complement fixation or precipitation can be produced with the same antigen and the same antibody by merely varying the proportions of the mixture. It is obvious, then, that the fact that complement fixation and precipitation do not run a parallel course affords no evidence of the separate existence of two varieties of antibody, namely, precipitins and amboceptors, for the proportions which favour the rapid formation of a large precipitate are unfavourable to the fixation of complement, and the proportions which effect the best fixation of complement do not lead to the rapid formation of a precipitate.

It will be remembered that in Wassermann and Bruck's experiment, the fresh bacterial extract had the power of producing a precipitate and of fixing complement. The extract was then put aside, and at the time of the second experiment it was found to have lost its precipitating powers without loss of its complement-binding properties. This result, can, I think, be explained without postulating the existence of two different antibodies. It seems probable that during the interval between the first and second experiments a destruction of the specific antigen had taken place, and that at the time of the second experiment

the antigen content of the extract had been so far reduced that there was no longer sufficient to produce a visible precipitate. The conditions were, nevertheless, exactly those which have been shown to be favourable to the fixation of complement—namely, the presence of a relatively small quantity of antigen and a relatively large quantity of antibody.

TABLE I.

Dilutions of normal Goat Serum (antigen)	(A) 1 in 10 dilution of Rabbit v. Goat Serum (antibody) Amount of precipitate formed	1 in 10 dilution of Rabbit v. Goat Serum (antibody)		
		(B) 0.05 c. c. guinea-pig complement	(C) 0.1 c. c. guinea-pig complement	(D) 0.2 c. c. guinea-pig complement
(1) 1 in 10	90			
(2) 1 in 20	60			
(3) 1 in 40	40			
(4) 1 in 80	45			
(5) 1 in 160	40			
(6) 1 in 320	30			
(7) 1 in 640	10			
(8) 1 in 1280	5			
(9) 1 in 2560	Large trace			
(10) 1 in 5120	Trace			
(11) 1 in 10240	nil			

A similar explanation probably holds good for some experiments of Liefmann and of Friedberger. In Friedberger's experiments the anti-serum was heated for one hour at 67° C., and was then found to have lost its precipitating property, but not its complement-fixing property. The effect of heating on the antiserum was probably to render the

precipitation process slow and incomplete. These are the very conditions under which complement is best fixed. Liefmann heated the antigen-containing serum and destroyed its power of forming a precipitate without interfering with its complement-binding power. This experiment is probably capable of a similar explanation.

With the majority of antisera investigated it was found possible to demonstrate that the proportions which rapidly produced a precipitate did not effectively bind complement. There were, however, two exceptions in the series. In the case of these antisera, which were both exceptionally "weak," the precipitate was only very slowly formed, even when large quantities of antigen were used. It was not found possible in these cases to find proportions of antigen and antibody which produced a precipitate without binding complement. With these antisera, in which precipitation was always slight and slow, the amount of complement fixed was always proportional to the degree of turbidity produced. If, however, the antiserum was a "good" antiserum, it was always found possible to prepare a mixture of antigen and antibody in proportions which would rapidly precipitate but which did not fix complement.

EXPERIMENT II (TABLE II).



























































































In this experiment the complement was added immediately and at varying periods after the mixtures of antigen and antibody were made.

Ten identical sets of antigen dilutions were prepared. To all the tubes was added the same amount of antiserum. One set was set aside for observations on the rate and degree of precipitation. Turbidity appeared immediately after mixing in the first four tubes. *After ten minutes* flocculi had appeared in the first three tubes, and tubes 4 and 5 showed turbidity. *After half an hour* large flocculi had separated, leaving a clear fluid in the first three tubes; tube 4 showed smaller flocculi, and tube 5 minute particles. Tube 6 showed marked uniform turbidity. Slight opalescence was present in 7 and 8. *After one hour* the precipitate had deposited in the first three tubes. In tubes 4, 5, and 6 smaller particles were still suspended in the fluid. Tubes 7 and 8 showed distinct turbidity, and a trace of opalescence could be detected in tube 9.

The other nine sets of tubes were treated as follows: To the first three sets complement in three different dilutions was added, and then to every tube the same amount of antibody. In the next three sets the antibody was added directly to the antigen, and the tubes were incubated

for half an hour. The complement was then added. In the next three sets the antigen and the antibody mixtures were incubated for one hour before the addition of complement. After the addition of complement each set of tubes was incubated for one hour, when a suitable mixture of corpuscles and hæmolytic serum was added. Each set was then incubated for a further period of one hour, at the end of which time the results were read and recorded. The experiment shows the result

TABLE II.
Antiserum 1 in 10 (Rabbit v. Goat)

Dilution of Goat Serum (antigen)	Complement added immediately			after ½ hr.			after 1 hr.		
	Fresh Guinea-pig Serum			0.05	0.1	0.2	0.05	0.1	0.2
(1) 1 in 10									
(2) 1 in 20									
(3) 1 in 40									
(4) 1 in 80									
(5) 1 in 160									
(6) 1 in 320									
(7) 1 in 640									
(8) 1 in 1280									
(9) 1 in 2560									
(10) 1 in 5120									

of adding complement at various times after the mixture of the antigen with the antibody. A full set of control tubes was also prepared. In all these tubes complete hæmolysis occurred.

Remarks on Table II.

It is quite apparent that to obtain the greatest fixation the complement should be present from the time when antigen is mixed with antibody. After half an hour's preliminary incubation there was a

marked reduction in the complement-binding power of the mixtures. If one hour was allowed to elapse before complement was added very little fixation took place. As was anticipated, this loss of complement-binding power was more marked in the tubes in which the precipitation process was rapid. A comparison of the results obtained in tubes 4 to 8 in the various columns shows this point clearly. With the immediate addition of complement the maximum fixation occurred in tube 5, which contained a mixture of 1 in 160 antigen with 1 in 10 antibody. When half an hour had been allowed to pass before complement was added, the contents of tube 5 showed little power to fix complement, while tube 6, which contained a mixture of 1 in 320 antigen with 1 in 10 antibody, showed the best fixation of complement. The experiment bears out the view that complement is not fixed to any extent by the particles of a visible precipitate. It is probable that complement is fixed during the very earliest stage of the precipitation process at a time when the individual aggregates are so small that no turbidity is visible. When, on the other hand, the process has advanced to a stage at which visible precipitation occurs, the conditions necessary for the fixation of complement are no longer present.

EXPERIMENT III (TABLE III).

In Experiment III the amounts of precipitate which occur when varying quantities of antigen are added to a constant quantity of antibody have been measured and are recorded in Table III.

The table shows that the amount of the precipitate formed depends on the relative proportions of antigen and antibody present in the mixture. With a 1 in 5 dilution of antiserum the largest precipitate was obtained by adding a 1 in 8 dilution of antigen. With half the quantity of antiserum (1 in 10) the largest precipitate was obtained by adding a 1 in 16 dilution of antigen. The largest precipitate obtained with the 1 in 10 dilution of antiserum was about half the largest amount obtained by the use of twice as much antiserum (1 in 5 dilution). This is in accord with the view of Chapman and Welsh that the amount of the precipitate is proportional to the amount of antiserum present. One of the main results of all these experiments was to show that for any quantity of antiserum there exists a quantity of antigen which is capable, within a definite period of time, of producing the largest precipitate obtainable from such a quantity of antiserum. Table III also illustrates very clearly the inhibitory effect of relative

excess of antigen. This is plainly seen by comparing the figures in the two columns. A 1 in 4 antigen dilution, which constituted a marked antigen excess for an equal quantity of 1 in 10 antiserum, produced almost the largest precipitate of the series when mixed with a 1 in 5 dilution of antiserum.

TABLE III.

	5 c.c. dilutions of normal horse serum (antigen)		5 c.c. of a 1 in 5 dilution of rabbit v. horse serum (antibody)	5 c.c. of a 1 in 10 dilution of rabbit v. horse serum	5 c.c. normal saline solution	
1	...	Undiluted serum	...	7.0	...	Clear
2	...	Diluted 1 in 2	...	14.0
3	...	" 1 in 4	...	19.0
4	...	" 1 in 8	...	20.0
5	...	" 1 in 16	...	11.0
6	...	" 1 in 32	...	6.0
7	...	" 1 in 64	...	4.0
8	...	" 1 in 128	...	3.0
9	...	" 1 in 256	...	2.0
10	...	" 1 in 512	...	1.0
11	...	" 1 in 1,024	...	0.75	...Less than 0.5...	..
12	...	5 c.c. normal saline solution	...	Clear	...	Clear

Three sets of dilutions of horse serum were prepared. To one set was added an equal quantity of a 1 in 5 dilution of antiserum, to another set was added a 1 in 10 dilution of the antiserum. The third set received an equal quantity of normal saline solution, and acted as an antigen control. The antiserum controls are shown in the tubes numbered 12. All the tubes were incubated for four hours at 37° C., and then placed overnight in the cold room. The tubes were then centrifugalized for one hour. The tubes ended in a narrow portion, which was calibrated in such a way that the amount of the precipitate could be accurately determined. The relative quantities of the precipitates in each tube are indicated by the figures.

EXPERIMENT IV (TABLE IV).

Experiment IV is designed to show more clearly the influence of excess of antigen on the resulting precipitate.

In the first two tubes the excess of antigen was so great that no trace of a precipitate appeared. In tube 3 the antigen was still present in relative excess although it contained only twice the optimal quantity of antigen. The effect of this excess was to render precipitation slow and imperfect. Opalescence only slowly made its appearance in this tube and after a considerable delay a few large flocculi became visible. Precipitation was even to the end of the experiment very incomplete and the contents of the tube remained permanently opalescent. It will be noticed that, if the proportions of antigen and antibody are approximately correct, precipitation rapidly proceeds by a process of aggregation

of particles to the formation of definite flocculi which fall to the bottom and leave a clear fluid. If there is a great excess either of antigen or antibody a condition of homogeneous turbidity or opalescence is the result.

The mixtures in which this slowing of precipitation is due to antibody excess have always very considerable power to bind complement. On the other hand, complement is not bound by mixtures in which antigen excess is responsible for imperfect precipitation. It will be seen from this and other tables that the precipitation reaction appears to be much more easily inhibited by excess of antigen than by excess of antibody. In Table IV, where the largest precipitate was produced by a 1 in 10 dilution, four times this quantity of antigen entirely inhibited the reaction, while a slight opalescence could be produced by the use of a one two-thousandth part of this quantity.

TABLE IV.—PRECIPITATION EXPERIMENT.



















		Dilutions of goat serum (antigen)			Rabbit v. goat serum (antibody) diluted 1 in 10
1	...	4 in 5	No deposit
2	...	2 in 5	No deposit
3	...	1 in 5	0.03
4	...	1 in 10	0.11
5	...	1 in 20	0.07
6	...	1 in 40	0.05
7	...	1 in 80	0.06
8	...	1 in 160	0.05
9	...	1 in 320	0.04
10	...	1 in 640	0.02
11	...	1 in 1,280	0.01
12	...	1 in 2,560	Large trace
13	...	1 in 5,120	Trace
14	...	1 in 10,240	No deposit; opalescent
15	...	1 in 20,480	No deposit; opalescent
16	...	1 in 40,960	No deposit; clear

The various amounts of antigen indicated in the table were mixed with a constant quantity of antiserum. The progress of precipitation was as follows: Immediately after mixing opalescence appeared in tubes 4 to 9. Small particles appeared after five minutes in tube 5, and shortly afterwards in tubes 4 and 6. After ten minutes big flocculi were present in tubes 4 and 5, and small flocculi in tube 6. After half an hour tubes 1 and 2 were still clear; tube 3 was opalescent; in 4, 5 and 6 large flocculi had fallen to the bottom of the tube, leaving a clear supernatant fluid; in 7 and 8 small particles were present; 9, 10 and 11 showed diminishing grades of uniform turbidity. After two hours tubes 1 and 2 were clear; in 3 a few flocculi had formed and fallen to the bottom, but the supernatant fluid was opalescent; in 4 to 11 the precipitate had settled to the bottom, leaving a clear supernatant fluid; 12 contained small particles still suspended in the fluid; 13 and 14 were distinctly opalescent, and 15 showed a trace of opalescence. After three hours the deposits were brought down by the centrifuge and their amounts recorded. Tubes 3, 14 and 15 remained opalescent after centrifugalization. Antigen and antibody controls were put up and remained clear.

EXPERIMENT V (TABLE V).

In this experiment an attempt has been made to show the effect of antigen excess in both precipitation and complement fixation. It will be seen that, as regards precipitation, the effect of the excess of antigen becomes more marked as the antiserum becomes more diluted. The complement fixation is more susceptible to the influence of antigen than the precipitation. There are two reasons for the inhibition of complement fixation by antigen excess which occur under two different

TABLE V.

Dilutions of Goat Serum (antigen)	Diluted 1 in 10		Antiserum Rabbit v. Goat Diluted 1 in 20		Diluted 1 in 40	
	Precipitation	Complement Fixation	Precipitation	Complement Fixation	Precipitation	Complement Fixation
(1) 1 in 10	Large Deposit		Trace Deposit		No Precipitate	
(2) 1 in 20	" "		Small Deposit		" "	
(3) 1 in 40	" "		Deposit		Trace Deposit	
(4) 1 in 80	" "		"		Very small Deposit	
(5) 1 in 160	" "		"		" " "	
(6) 1 in 320	Deposit		"		" " "	

For the sake of simplicity the controls have been omitted from the table. All the usual control tubes were set up and were satisfactory. Six sets of antigen dilutions were put up. Three sets were reserved for the precipitation experiment and three sets for the complement fixation experiment.

sets of conditions. With great antigen excess no precipitation occurs; the mixture remains clear, and no complement is fixed. With a less quantity of antigen a large precipitate is formed. These are the conditions which, as has already been shown, are most favourable to the formation of a precipitate, but which do not favour the fixation of complement. If a long series of tubes is prepared in which various amounts of antigen are mixed with a constant amount of antibody,

a variety of zones may be differentiated. The largest amounts of antigen entirely inhibit both precipitation and complement fixation and the mixture remains clear. In the next zone precipitation is delayed and incomplete, and no complement is fixed. In the third zone precipitation is rapid and complete, but no complement is fixed. In the fourth zone precipitation begins again to be delayed and is less complete. These proportions represent *for precipitation* a slight antibody excess, nevertheless, it is in this zone that complement fixation appears and reaches its maximum. In the fifth zone precipitation is greatly delayed and is very incomplete. In this zone complement fixation is well marked, but nevertheless decreases tube by tube with the precipitate. In the sixth zone complement fixation can be demonstrated for a variable number of tubes after all evidence of precipitation has disappeared.

EXPERIMENT VI (TABLE VI).

This experiment is designed to show that similar inhibition phenomena occur in reactions between bacterial antigen and its corresponding antibody. It might be supposed that the inhibitory influence in the precipitate formation shown in the first three tubes of the experiment recorded in Table IV was due not so much to excess of specific antigen as to the presence of a relatively large amount of colloidal material or to a relatively small quantity of electrolytes. The antigen employed in this case was a distilled water extract of *Bacillus typhosus*. This extract contained very little proteid, and the fact that with this extract it was possible to demonstrate the influence of antigen excess is evidence that the inhibition is really due to an excess of the actual antigen.

In other respects Table VI shows the same points as Table III. The influence of the relative proportions of antigen and antibody on the amount of the precipitate is well shown. The method employed for measuring the amount of the precipitate was not, of course, extremely accurate, nevertheless the figures are sufficiently close to lend considerable support to the views of Chapman and Welsh. It will be seen from tube 2 that a mixture of 1 in 2 antigen with 1 in 5 antiserum produced a precipitate of 8. Tube 4 shows that a mixture of one quarter of the amount of antibody with one quarter of the amount of antigen produced one quarter of the amount of precipitate.

TABLE VI.

	5 c.c. dilutions of extract of <i>Bacillus typhosus</i> (antigen)	5 c.c. of a 1 in 5 dilution of anti- typhoid serum (antibody)	5 c.c. of a 1 in 20 dilution of antityphoid serum	5 c.c. normal saline solution (extract controls)
1 ...	Undiluted	15.0	... Very slight trace ...	Clear
2 ...	Diluted 1 in 2	8.0	... 1.0
3 ...	" 1 in 4	6.0	... 3.0
4 ...	" 1 in 8	3.0	... 2.0
5 ...	" 1 in 16	1.5	... 1.0
6 ...	" 1 in 32	0.75	... 0.5
7 ...	" 1 in 64	0.5	... 0.25
	Serum controls—			
8 ...	5 c.c. normal saline solution	Clear	... Clear ...	—

* Three sets of dilutions of typhoid extract were prepared. To the first set was added an equal quantity of a 1 in 5 dilution of antityphoid serum; to the second set was added a 1 in 20 dilution; to the third set normal saline. The tubes were incubated for three hours, and then allowed to stand overnight in the cold room. On the next day the precipitate was brought down with a centrifuge and the amount of each precipitate was recorded.

ON THE QUANTITATIVE RELATIONS OF ANTIGEN AND ANTIBODY IN PRECIPITATION AND COMPLEMENT FIXATION EXPERIMENTS.

* It will be seen from the experiments which have been described that the question of the relative proportions of antigen and antibody is one of the greatest importance in both the precipitation and the complement fixation reaction. Chapman and Welsh have shown that from any given quantity of antiserum a certain definite quantity of precipitate can be obtained. According to their view, the amount of precipitate is directly proportional to the amount of antiserum present. If to a constant quantity of antiserum are added various quantities of antigen the amount of the precipitate will in all cases be the same, provided that sufficient time be allowed for complete precipitation to take place. The larger quantities will rapidly precipitate the precipitable substance of the antiserum and the smaller quantities will precipitate it very slowly, but ultimately the same amount of precipitate will be produced.

In the experiments described in this paper precipitation has only been allowed to proceed for a limited time. When a short time only is allowed for precipitation, the results necessarily differ widely from the figures obtained by Chapman and Welsh. When only a short time is allowed, the amount of the precipitate depends on the relative proportions of antigen and antibody; that is to say, for any given quantity of antiserum a quantity of antigen can be found which is able rapidly to precipitate the precipitable substance in the given quantity of antiserum.

Such a mixture may be said to contain antigen and antibody in optimal or equivalent proportions. In such a mixture particles appear almost immediately, and after a few minutes large flocculi have aggregated together and fallen to the bottom of the tube, leaving a perfectly clear supernatant fluid in which apparently no further precipitate is formed. The whole process is under these conditions complete within a few minutes.

The importance of equivalent proportions of antigen and antibody for precipitation is fairly well shown in Tables III and VI.

If a series of quantities of antigen are mixed with a constant amount of antiserum and if the mixtures are centrifugalized after a few hours, it is found that for any given quantity of antiserum there exists a quantity of antigen which is able to produce the largest precipitate. If to a duplicate series of amounts of antigen there be added half the amount of antiserum, the largest precipitate will be half the amount of the largest precipitate of the first series, and it will be found in the tube which contains half the amount of antigen which produced the largest precipitate in the first series.

The amount of the precipitate can be shown to be proportional to the amount of antiserum (1) by adding any amount of antigen and waiting until precipitation is complete; (2) within a shorter period of time by adding the optimal amount of antigen.

In complement fixation the matter of equivalent proportions is of even greater importance, for it is essential that the experiment be carried out within a comparatively short period of time. It has been shown that the proportions of antigen and antibody which produce the most effective precipitation are not, as a rule, those which produce the greatest fixation of complement. For any quantity of antiserum it is generally possible to select two quantities of antigen, the one will produce the most rapid and complete precipitation, the other the greatest fixation of complement. The quantity which produces the best precipitation is many times greater than the quantity which produces the best fixation of complement. The fixation of complement is, in fact, dependent on two factors—the one is the amount of the precipitate, the other is the state of division of the particles of the precipitate, or rather the rate at which the precipitate is formed. The amount of complement fixed is proportional to the amount of the precipitate, provided that the precipitate is slowly formed. To show that the amount of complement fixed is proportional to the amount of antiserum present, it is obviously necessary to add to each quantity of antiserum the optimal quantity of antigen.



















































ON THE USE OF OPTIMAL PROPORTIONS IN THE PRACTICAL
APPLICATION OF THE COMPLEMENT FIXATION TEST.

Experiment VII and Experiment VIII (Tables VII and VIII).

It has been shown that complement is best fixed when antigen and antibody are mixed in optimal proportions which have to be determined for any antigen and antiserum by actual experiment.

The experiments recorded in Tables VII and VIII show fairly clearly the inhibitory influence of the presence of a relative excess

TABLE VII.

Dilutions of Typhoid Extract	Antityphoid Serum diluted 1 in 5	Diluted 1 in 50	Diluted 1 in 100	Diluted 1 in 300	Normal Saline Solution Extract Control.
(1) 1 in 4					
(2) 1 in 8					
(3) 1 in 16					
(4) 1 in 32					
(5) 1 in 64					
(6) 1 in 128					
(7) 1 in 256					
(8) 1 in 512					
(9) 1 in 1024					
(Serum Controls)					
10)					

The results shown in this table were obtained by mixing nine quantities of an extract of *Bacillus typhosus* with four quantities of an antityphoid serum. The extract and serum were the same as those used in the precipitation experiment recorded in Table VI. This experiment was carried out in the same manner as Experiment VIII. (See footnote to Table VIII.)

either of antigen or of antiserum. The complement fixation reaction is frequently used for the purpose of detecting the presence of antigen or antibody, for the purposes of diagnosis. If the material which is being investigated contains only a trace of the specific antigen, its presence can only be demonstrated by adding an approximately equivalent quantity of antiserum. For instance, it will be seen in Table VIII that the presence of antigen in an extract dilution of 1 in 1,280 could only be demonstrated by adding an antiserum dilution of 1 in 20; smaller and larger quantities of the antiserum failed to show any fixation of complement. Table VII shows that when the antiserum was diluted to 1 in 300 it was necessary to dilute the extract considerably (1 in 32) before any marked fixation of complement could be demonstrated.

Since the correct proportions must in every case be ascertained by direct experiments, it follows that it is advisable to use many quantities both of the antigen and of the antiserum if it is desired to detect the presence of a minute trace of either.

The complement fixation method is often used for the quantitative estimation both of antigen and of antibody. It has been recommended as a method of determining the "strength" of antimeningococcus serum, and efforts have been made to devise a method for giving a quantitative value to the results of the Wassermann reaction. In one method a constant quantity of the antigen is selected and titrated with falling quantities of antiserum. The probable result of this method is seen in Table VII. If a 1 in 8 dilution of extract has been selected as the constant quantity of antigen, the limit of the antiserum is reached at a dilution of 1 in 100. Had a 1 in 32 dilution of extract been selected, the limit would not have been reached until the antiserum had been diluted to 1 in 300. The apparent titre of the antiserum is in fact determined by the quantity of extract (antigen) selected.

The other method is to keep the dilution of antiserum constant, and to use falling dilutions of the extract. The results to be expected from this method are shown in Table VIII.

It will be seen from this experiment that if an antiserum dilution of 1 in 5 was taken, the extract could be diluted to 1 in 320, but if the antiserum dilution selected was 1 in 20 the extract could be diluted to 1 in 1,280. The result arrived at is that the serum dilution 1 in 20 is stronger than the serum dilution 1 in 5. If we suppose that the 1 in 5 serum dilution represents a constant quantity of an antiserum A, and that the 1 in 20 dilution represents an equal quantity of another

antiserum, we arrive by this method at a result which shows that antiserum B is stronger than antiserum A. It is equally obvious that the strength of the extract could not have been determined either by taking a constant amount of extract and falling quantities of antiserum or by taking a constant amount of antiserum and titrating it with falling quantities of extract.

TABLE VIII.

Dilutions Typhoid Extract.	Dilutions of Antityphoid Serum							Normal Saline Extract Control.
	1 in 5	1 in 10	1 in 20	1 in 40	1 in 80	1 in 160	1 in 320	
(1) 1 in 5								
(2) 1 in 10								
(3) 1 in 20								
(4) 1 in 40								
(5) 1 in 80								
(6) 1 in 160								
(7) 1 in 320								
(8) 1 in 640								
(9) 1 in 1280								
(10) 1 in 2560								
Serum Controls								

In this experiment ten dilutions of a typhoid extract and seven dilutions of an antityphoid serum were used. Every dilution of extract was allowed to interact with every dilution of antiserum. Each tube contained 0.5 c.c. of an antiserum dilution, 0.5 c.c. of an extract dilution, and 0.5 c.c. fresh guinea-pig serum in a dilution of 1 in 10. After incubation for one hour at 37° C. there were added 0.5 c.c. of a 1 in 20 suspension of sheep corpuscles and 0.5 c.c. of a 1 in 400 dilution of hæmolytic serum (rabbit v. sheep). The results were read after a second period of incubation for two hours. The extract and serum were different from those used in Experiment VII.

As far as these experiments go it appears that if a constant quantity of extract be added to varying quantities of antiserum valid *relative* differences can be obtained between two given sera. If, however, varying quantities of extract be added to a constant quantity of antiserum a greatly diluted antiserum can be shown to be stronger than the one which has been less diluted.

To make an absolute quantitative estimation either of the antibody content of an antiserum or of the antigen content of an extract it is necessary to titrate falling quantities of antiserum with falling quantities of the extract.

If it be desired to determine the absolute complement-binding power of any quantity of antiserum it is essential to mix with it the equivalent amount of extract. When the correct proportions have been determined the amount of complement bound may be estimated by the use of various amounts of complement. The value of using various amounts of complement as a quantitative method was pointed out by Muir and Martin (1906). The actual complement-binding power of any amount of antiserum can, however, only be determined if it is mixed with the correct amount of extract.

ON THE CAUSE OF THE INHIBITION OF THE REACTION BY RELATIVE EXCESS OF EITHER ANTIGEN OR ANTIBODY.

No theory of the cause of complement fixation can be considered satisfactory which does not explain the inhibition effects produced by relative excess of either antigen or antibody. It seems rather a difficult matter to interpret these effects on the basis of the amboceptor hypothesis. The only possible explanation would be similar to that offered by Neisser and Wechsberg (1901) in their paper on bacteriolysis.

It will be remembered that in their experiments, when a large quantity of antiserum was present no bacteriolysis took place. Neisser and Wechsberg put forward the view that under these circumstances the mixture contained a large excess of free amboceptors, that is to say, amboceptors which had not become attached to the bacilli. They assumed that these free amboceptors took up a large quantity of the complement, with the result that there was not sufficient complement for the amboceptors which had attached themselves to the bacilli. It does not seem easy to apply this highly theoretical explanation to the effects shown in Tables VII and VIII. If it is assumed that in this case the complement is deviated by the excess of free amboceptors, it

is also necessary to assume that the complement is subsequently liberated from the free amboceptors, to be taken up by the combination of hæmolytic amboceptors and red corpuscles. The amboceptor hypothesis, moreover, leaves us without any explanation of the inhibition produced by a relative excess of extract.

Now it has been shown that when either antiserum or antigen is present in relative excess, precipitation is very greatly delayed. Under these conditions the aggregation process necessary to complement fixation does not occur, or at any rate does not occur within the hour allowed for the reaction. The precipitation theory affords a much better explanation of the excess effects than the amboceptor theory. As has already been pointed out, excess of antigen interferes with the fixation of complement in two ways. If the excess is very great no precipitate is formed, and no complement fixed. With less quantities of antigen a stage can, as a rule, be demonstrated, in which the precipitation occurs so rapidly that the early stages, during which complement is probably fixed, are passed through too rapidly to permit of effective fixation taking place.

THE QUANTITATIVE ESTIMATION OF SERUM IN THE WASSERMANN REACTION (TABLE IX).

This experiment has been recorded in order to show that excess effects can be demonstrated with a positive syphilitic serum, and an extract of syphilitic liver. It will be seen that an accurate quantitative result cannot be obtained either by titrating a constant quantity of extract with falling amounts of serum, or by keeping the serum constant, and varying the quantities of extract.



































The point raised is fairly well shown in Table IX. If a dilution of 1 in 10 extract had been selected as the constant quantity, it would have been found that a "complete reaction" could be obtained after the serum had been diluted to 1 in 20. If, however, half the quantity of extract had been selected, a practically complete reaction would have been obtained after the serum had been diluted to 1 in 40. It will be seen that the extent to which the serum can be diluted depends on the dose of extract selected.

The table also shows the result of using a constant amount of serum and falling amounts of extract. If we take two dilutions of serum, 1 in 5 and 1 in 20, and titrate each quantity with various quantities of the extract, we find that, using the 1 in 20 serum

dilution, the extract can be diluted further than it can be if a 1 in 5 dilution is used.

If these two dilutions of serum, 1 in 5 and 1 in 20, be taken as representing two separate sera, which are to be investigated, and if a constant quantity of each is titrated with falling quantities of extract, it is obvious that an incorrect result will be obtained.

TABLE IX

Dilutions of Syphilitic Serum	Dilutions of Liver Extract.				Saline Serum Controls
	1 in 10	1 in 20	1 in 40	1 in 80	
1 in 5					
1 in 10					
1 in 20					
1 in 40					
1 in 80					
1 in 160					
Saline Extract Controls					

The materials used for this experiment were the serum from a syphilitic patient and an alcoholic extract prepared from the liver of a syphilitic fetus. Each tube (excepting, of course, the control tubes) contained 0.5 c.c. of diluted extract, 0.5 c.c. of diluted serum, and 0.5 c.c. of guinea-pig serum diluted 1 in 10. After one hour's incubation at 37° C. there were added 0.5 c.c. of a 1 in 20 suspension of sheep corpuscles and 0.5 c.c. of a 1 in 500 dilution of hæmolytic serum. The results were read after a second period of incubation lasting for one hour.

To obtain an accurate quantitative result, various quantities of extract must be mixed with various quantities of serum. When the optimal proportions have been ascertained the actual amount of complement fixed can be determined by the use of various quantities of complement.

Apart from the question of attempting to make the Wassermann

reaction quantitative, it is certainly advantageous at all times to use a series of dilutions. It will be seen from the table that a 1 in 40 dilution of serum gives a marked fixation of complement with an extract dilution of 1 in 20, but only partial fixation with an extract dilution of 1 in 10.

EXPERIMENT X (TABLE X).

This experiment is similar to those shown in Tables VII and VIII. Seven quantities of typhoid extract and six quantities of antityphoid serum were used. The experiment was set up in such a way that every quantity of extract was mixed with every quantity of antiserum. There resulted forty-two mixtures, each containing different proportions of antigen and antibody. Each of these mixtures was represented by three tubes, each of which received a different dose of complement. A quantitative measure of the amount of complement bound by each of the mixtures was thus attempted. The value of the complement was determined by a separate experiment, and the minimal hæmolytic dose of the guinea-pig serum was found to be 0.0125 c.c. The method is of course only roughly quantitative, for it must not be assumed that 0.025 c.c. has *exactly* twice the complement value of 0.0125 c.c. of the guinea-pig serum. The method was nevertheless sufficiently accurate to give comparative results of some interest.

In the first three columns corresponding to the larger amounts of antiserum the quantities of complement used were 0.2 c.c., 0.1 c.c., and 0.05 c.c. In the three last columns corresponding to the smaller amounts of antiserum the amounts of complement were 0.1 c.c., 0.05 c.c., and 0.025 c.c. The experiment was performed in essentially the same way as in the case of the other experiments described in this paper. The extract dilutions were first prepared, the complement was added next, and finally the antiserum. After one hour's incubation at 37° C. the blood and hæmolysin were added. After a further period of incubation (two hours) the results were read. As in all the other experiments, each of the five ingredients was added in a bulk of 0.5 c.c., and the total quantity of fluid in each tube was thus 2.5 c.c.

It will be seen that the larger quantities of extract spontaneously bound the smallest quantity of complement used. The extent to which this spontaneous binding occurred is shown in the extract control column, and as a matter of fact, the result of the experiment was not in the least obscured.

Remarks on Table X.—The Relation between the Amount of Antiserum and the Amount of Complement Fixed.

This experiment demonstrates once more the importance of optimal proportions of antigen and of antibody.

					Extract
0.0125 c.c. antiserum bound most complement when mixed with					0.05 c.c.
0.00625	"	"	"	"	0.05 or 0.025 c.c.
0.003125	"	"	"	"	0.025 or 0.0125 c.c.
0.0015625	"	"	"	"	0.0125 c.c.
0.00078125	"	"	"	"	0.00625 c.c.
0.000390625	"	"	"	"	0.003125 c.c.

That is to say, as the amount of antiserum was diminished the amount of extract necessary to give the best results also diminished. It is, in fact, quite impossible to estimate the antibody content of any given amount of serum, unless the correct amount of antigen is used. With the data provided by Table X it is, however, possible to form a rough estimation of the amount of complement bound by each quantity of antiserum.

By selecting (in Table X) the most effective dose of extract for each quantity of antiserum it is possible to roughly determine the complement bound in each case.

It will be seen that the amount of complement bound is approximately proportional to the amount of antiserum. It is probable that when antiserum and antigen are mixed in the proportions most favourable to complement fixation that the amount of complement fixed is in proportion to the amount of antiserum. This is in close agreement with the results of the precipitin experiments, in which it is shown that the amount of precipitate is in proportion to the amount of antiserum, provided that antigen and antiserum are mixed in equivalent proportions.

THE RELATIVE ADVANTAGES OF THE PRECIPITATION AND COMPLEMENT FIXATION METHODS.

From the time of its first introduction by Neisser and Sachs, the complement fixation method has been generally considered to possess several advantages over the precipitation method. It is, in the first place, the more delicate test for the presence of a minute trace of antigen. It has also been pointed out that the results obtained are more easily observed, for the absence of hæmolysis is more easily

determined than the presence of a faint trace of opalescence or turbidity. There is, moreover, the great advantage that a perfectly clear solution of antigen is not an absolute essential. Besides these merits, which are sufficiently well known, the complement fixation method is superior to the precipitation method, in that it allows of a finer differentiation of nearly allied bacteria, and of the sera of nearly allied animals. With both methods group reactions not infrequently cause considerable difficulty, but with the complement fixation method there are two ways in which these difficulties can to a great extent be overcome.

The first of these ways consists in diluting the antiserum until a dilution is obtained which no longer gives the group reaction. This procedure is often impossible with the precipitation test, for the precipitate is derived from the antiserum, and if the antiserum is greatly diluted the precipitate is so reduced that it is no longer visible. For practical purposes differentiation can only be obtained with the precipitation method by greatly diluting the antigen. The complement fixation method permits extreme dilution both of antigen and antiserum.

The other method, by which the group reaction may be eliminated, is by increasing the amount of complement. For instance, a mixture of human serum with the antiserum derived from a rabbit which has been injected with human serum absorbs complement, but a mixture of monkey serum with the same antiserum (rabbit v. man) also absorbs complement. By using various amounts of complement, it can be shown that a mixture of human serum with rabbit v. man antiserum absorbs more complement than a mixture of monkey serum with rabbit v. man antiserum.

It is also frequently possible to eliminate a group reaction by using larger quantities of the hæmolytic antiserum.

Examples of the effect of varying the quantities of antiserum and of complement are given in the following tables.

Remarks on Tables XI, XII and XIII.

For these experiments rabbits were immunized with normal human serum and with normal monkey serum (*Macacus rhesus*). The antisera obtained were not very powerful, but served, nevertheless, to demonstrate the points which have been mentioned.

Table VIII shows the results of a precipitation experiment. Both

sera produced marked precipitates with the 1 in 2½ and the 1 in 10 dilutions of the antihuman serum. The precipitates produced by the human serum were somewhat more marked than those produced by the monkey serum, but the difference was insignificant. When the antiserum was used in a dilution of 1 in 40 precipitation practically ceased. In Table XII a complement fixation experiment is shown. In this case, too, the 1 in 10 and 1 in 20 dilutions of the antisera failed to bring out any striking difference between human serum and monkey serum. When, however, the antisera were diluted to 1 in 40 and 1 in 80 a perfectly satisfactory differentiation was obtained.

TABLE XI.—PRECIPITATION EXPERIMENT.

	Dilution of normal human serum	Rabbit v. man serum diluted			
		1 in 2½	1 in 10	1 in 40	1 in 160
1	1 in 100	Large deposit	Deposit	Slight deposit	Nil
2	1 in 200	"	"	Trace	"
3	1 in 400	"	"	Nil	"
4	1 in 800	"	"	"	"
5	1 in 1,600	Small deposit	Trace	"	"
6	1 in 3,200	Trace	Nil	"	"
7	1 in 6,400	Nil	"	"	"
	Dilution of monkey serum (<i>Macacus rhesus</i>)				
		1 in 2½	1 in 10	1 in 40	1 in 160
1	1 in 100	Large deposit	Deposit	"	"
2	1 in 200	"	"	"	"
3	1 in 400	"	"	"	"
4	1 in 800	Small deposit	Trace	"	"
5	1 in 1,600	Trace	Nil	"	"
6	1 in 3,200	Nil	"	"	"
7	1 in 6,400	"	"	"	"

Various dilutions of normal human serum and of monkey serum were mixed with antihuman serum in four dilutions. The resulting precipitates are indicated in the table.

In the experiment recorded in Table XIII the same antisera were employed as of Table XII. In Table XII it was shown that the 1 in 10 dilutions of the antisera showed no distinction between human serum and monkey serum. In Table XII the usual quantity of complement, 0.5 c.c. of a 1 in 10 dilution of guinea-pig serum, was employed. In Table XIII twice this quantity was used, with the result that a marked differentiation was obtained.

When it is desired to differentiate between the sera of closely allied animals, the complement fixation method is to be preferred to the precipitation method. The results of the complement fixation experiment are, to a great extent, under the control of the worker. In the first place, it is possible, by varying the amount of complement, to

estimate quantitatively the complement-binding power of various antigen and antibody mixtures. It is also possible to control the degree of hæmolysis by varying the amount of the hæmolytic serum used, and by varying the time of the second period of incubation during which the hæmolysis takes place. These methods of modifying the result are often extremely useful when a fine degree of differentiation is required.

The great advantage, however, which the complement fixation method possesses is that it permits of the employment of many dilutions of antiserum. With the precipitation method the only possible way is to take a fixed dose of antiserum, and titrate it with falling doses of the antigen. The complement fixation method permits the use of various quantities, not only of antigen but of antiserum. By selecting a suitable quantity of antiserum a group reaction can be, as a rule, eliminated.

















































































DISCUSSION OF RESULTS.

The evidence for the separate identity of complement-binding antibodies and precipitins has been given at some length in the early portion of this paper. There is only need to take up the principal arguments and examine them in relation to the present experiments.

(1) *Many instances have been recorded in which there has appeared to be no relation between the amount of precipitate formed and the amount of complement fixed: (a) either a large precipitate has formed and no complement has been fixed, (b) or a slight opalescence has been observed or perhaps no precipitate at all, but complement has been very efficiently fixed.*

Now it has been shown that by taking any one antigen and any one antibody, and by simply varying their relative proportions, it is possible to produce either precipitation without complement fixation, or complement fixation without precipitation. If the proportions are so adjusted that the precipitate is rapidly formed, little or no complement is bound, but if the proportions are such that precipitation is slow and incomplete, nothing more than a slight opalescence may appear, even after the lapse of hours; complement is, nevertheless, efficiently fixed. The amount of complement absorbed is conditioned by two factors—amount of precipitate formed and the rate of its formation. If the precipitate is very rapidly formed no complement is fixed, but if the formation of a precipitate is sufficiently slow the amount of complement absorbed is always found to be proportional

TABLE XII.

COMPLEMENT FIXATION EXPERIMENT				
Dilutions of Normal Human Serum	1 in 10	1 in 20	1 in 40	1 in 80
(1) 1 in 200				
(2) 1 in 400				
(3) 1 in 800				
(4) 1 in 1600				
(5) 1 in 3200				
Dilutions of Normal Monkey Serum (Macacus Rhesus)				
(1) 1 in 200				
(2) 1 in 400				
(3) 1 in 800				
(4) 1 in 1600				
(5) 1 in 3200				
Dilutions of Normal Human Serum				
(1) 1 in 200				
(2) 1 in 400				
(3) 1 in 800				
(4) 1 in 1600				
(5) 1 in 3200				
Dilutions of Normal Monkey Serum (Macacus Rhesus)				
(1) 1 in 200				
(2) 1 in 400				
(3) 1 in 800				
(4) 1 in 1600				
(5) 1 in 3200				

Various dilutions of normal human serum and normal monkey serum (*Macacus rhesus*) were mixed with various dilutions of rabbit v. man and rabbit v. monkey antisera. 0.5 c.c. of the antigen dilution was mixed with 0.5 c.c. of the antiserum dilution and 0.5 c.c. of a 1 in 10 dilution of fresh guinea-pig serum. This 1 in 10 dilution of guinea-pig serum was shown to contain two hemolytic doses of complement. After incubation for one hour sheep corpuscles and hemolytic serum were added, and the tubes were incubated for a further period of one hour. The usual controls, designed to show that none of the sera used had an anti-complementary action, were also done, but are not shown in the table.

to the amount of the precipitate. In the case of most antisera it is possible to demonstrate either marked precipitation with little or no complement fixation, or complement fixation with little or no precipitation. Some antisera, however, are in all dilutions and proportions very slowly precipitated, and in these cases the amount of precipitate is always proportional to the amount of complement fixed. The fact that complement fixation occurs without the formation of a visible precipitate, and a bulky precipitate may form without complement being fixed, cannot be accepted as evidence that the two reactions depend on the existence of two separate antibodies.

(2) *Complement fixation can be demonstrated in mixtures which contain so minute a quantity of antigen that no trace of a precipitate can be detected.*

That a trace of antigen can be detected by the complement fixation method when no trace of a precipitate can be seen is almost universally admitted. This fact, however, is no evidence that precipitation and complement fixation are independent phenomena. When only a trace of antigen is present the precipitation process is incomplete and extraordinarily slow. Now it has been shown that it is during the very earliest stages of the reaction between antigen and antibody that complement is best fixed. There is, indeed, reason for thinking (Table II) that the greater part of the complement is fixed during the earliest period of the reaction before even a trace of opalescence makes its appearance.





























(3) *By heating the antiserum or the antigen containing serum, or by merely storing an extract, the power of forming a precipitate is destroyed while the power of binding complement is retained.*

A similar explanation to that offered in the last paragraph may reasonably be given. When a bacillary extract is stored away a gradual loss of specific antigen may be supposed to occur. The old extract is no longer able to produce rapidly an obvious precipitate, but is only able to precipitate the antiserum slowly and incompletely. These are just the conditions which favour complement fixation. Heat probably acts by altering either antigen or antibody, so that precipitation is slower and less complete, and consequently favourable to the fixation of complement.

(4) *The serum of an animal during the process of immunization develops complement-binding properties earlier than the power of forming a precipitate.*

This is exactly the result that might be anticipated. The more

TABLE XIII.
COMPLEMENT FIXATION EXPERIMENT

Dilutions of Normal Human Serum	Antiserum Rabbit v. Man Diluted 1 in 10	Antiserum Rabbit v. Monkey Diluted 1 in 10
(1) 1 in 100		
(2) 1 in 200		
(3) 1 in 400		
(4) 1 in 800		
(5) 1 in 1600		
(6) 1 in 3200		
(7) 1 in 6400		
Dilutions of Normal Monkey Serum (Macacus Rhesus)		
(1) 1 in 100		
(2) 1 in 200		
(3) 1 in 400		
(4) 1 in 800		
(5) 1 in 1600		
(6) 1 in 3200		
(7) 1 in 6400		

In this experiment all the materials used were exactly the same as those used in Experiment XII. The only difference is that exactly twice as much complement was used. In Experiment XII the usual dose of complement, guinea-pig serum in a dilution of 1 in 10, was used. In Experiment XIII a 1 in 5 dilution of guinea-pig serum was used and complete differentiation obtained.

delicate reaction is, as might be supposed, the first to make its appearance. The slight aggregation of particles which follows the mixture of antigen and "weak" antiserum is not sufficient to produce a visible precipitate, but can be demonstrated by the complement fixation reaction.

It should also be remembered that the common method of determining the titre of a precipitin serum is to take a constant amount of the antiserum, usually quite a large amount, and to test it with falling quantities of the antigen. For determining the complement-binding value of a serum the reverse method is commonly used—that is to say, a constant amount of antigen is mixed with falling quantities of antiserum. In such experiments the result is dependent on the relative proportions of antigen and antibody. If the complement-binding and precipitate-forming properties are compared, the dilutions, relative proportions, and the times allowed for the reactions are usually different. Under such conditions it is not surprising that the complement binding properties are earlier demonstrable than the precipitating properties or the reverse. The results are dependent on the experimental conditions.

The fact that Chapman and Welsh have been able to prove that the precipitate is derived from the antiserum has an important bearing on the relation between precipitate formation and complement fixation. When it was held that the precipitate was derived from the antigen it was difficult to see how the precipitate obtained from an exceedingly minute trace of antigen could be effective in complement fixation. Chapman and Welsh have shown that it is the antigen which precipitates the antiserum, and that a very minute trace of antigen is able, if sufficient time is allowed, to precipitate a relatively enormous precipitate from the antiserum. The action of the antigen is to induce an aggregation of the molecules of the antiserum, and the earlier stages of this process produce the effective conditions for complement fixation. It is probable that the researches of Chapman and Welsh will prove of value in helping to explain the mechanism of other serum reactions.

It has been shown that the greater part of the complement is bound at a very early stage in this aggregation process. Indeed, after a visible opalescence has once formed it seems that very little complement is taken up. The fixing of complement is probably an adsorption process for which the optimal conditions are afforded during the earlier stages of precipitation. This view is supported by the results obtained in Experiment II.

Chapman and Welsh have shown that the amount of precipitation which can be obtained from any given quantity of antiserum is a constant quantity which is independent of the quantity of antigen which may be present. This result is obtained if sufficient time be allowed for complete precipitation. The rate, however, at which precipitation takes place is closely dependent on the amount of antigen present. If precipitation is interrupted after a few hours, the amount of the precipitate formed bears a direct relationship to the amount of antigen present.

In complement fixation experiments the reaction which takes place in the first hour which follows the mixture of antigen and antibody is alone of importance. If a constant quantity of antiserum be mixed with a series of quantities of antigen, a quantity of antigen can be selected which gives the largest precipitate within the time-limit of the experiment. Such a quantity of antigen may be called the optimal quantity of antigen, because it is the quantity which acts the most rapidly and efficiently on the selected quantity of antiserum. Such quantities of antigen and antiserum may be said to be the optimal proportions for precipitation.

The relation of the amount of complement fixed to the amount of precipitate formed is complicated by the influence of another factor, the rate at which precipitation takes place. The conditions under which complement fixation takes place are those under which the presence of a relative excess of antiserum produces slow and incomplete precipitation. Provided that the mixture contains a sufficient excess of antiserum, it is true that the amount of complement fixed is proportional to the amount of precipitate formed, but if the proportions are such that precipitation is rapid, then little or no complement is fixed. These experiments offer an explanation of the contradictory results which have been published, for the question as to whether a relation can be demonstrated between the amount of precipitate formed and the amount of complement fixed depends on the relative proportions of antigen and antibody.

The proportions, in fact, which favour rapid and complete precipitation are positively unfavourable to complement fixation. On the other hand, there is a definite relation between the proportions most favourable to precipitation and those most favourable to complement fixation. If a constant amount of antiserum be taken it will, in the majority of cases, be found that the amount of antigen which will produce the best complement fixation is many times less than the amount

necessary to produce the largest precipitate. The reason why the two reactions do not run a parallel course is not because they are caused by two different sets of antibodies, precipitins and amboceptors, but because they represent two phases or two stages of the same reaction, and it is not possible to demonstrate both stages under the same conditions. A flocculent precipitate represents the complete and final stage of a change which can be recognized in its earliest and incomplete stage by means of the complement fixation method.

SUMMARY AND CONCLUSIONS.

(1) The mixture of equivalent proportions of antigen and antibody results in the rapid formation of the largest precipitate which can be obtained from any given quantity of antiserum.

(2) When the mixture contains an excess either of antigen or antibody, precipitation is delayed.

(3) Great excess either of antigen or of antibody entirely inhibits the formation of a precipitate.

(4) When antigen and antibody are mixed in the proportions which rapidly form a large precipitate very little or no complement is fixed. There is, under these conditions, no relation between the amount of precipitate formed and the amount of complement fixed.

(5) In mixtures in which precipitation is delayed by a relative excess of antibody there is a marked fixation of complement.

(6) The most marked fixation is obtained by mixing definite proportions of antigen and antibody.

(7) If a constant quantity of antibody is added to a series of quantities of antigen, two quantities of antigen can be selected. The one quantity is that which produces the largest precipitate, the other quantity is that which produces the greatest fixation of complement. The mixture which produces the greatest fixation of complement always contains considerably less antigen than the mixture in which the largest precipitate is produced.

(8) Relative excess either of antigen or antibody results in a decrease in the amount of complement which is fixed. If the mixture contains antigen in excess of the amount most favourable to the fixation of complement, precipitation is more rapid, but less complement is fixed. With a further increase in the relative amount of antigen precipitation is also inhibited. If, however, the amount of antigen is less than that which produces the best fixation of complement there is a diminution

not only in the amount of complement fixed, but also in the amount of the precipitate. With a further decrease of antigen both reactions steadily decrease until a dilution is reached at which visible precipitation ceases while a certain degree of complement fixation remains.

(9) In mixtures in which precipitation is sufficiently delayed by relative antibody excess the amount of complement fixed bears a direct relationship to the amount of precipitate formed.

(10) Provided that antiserum and antigen are mixed in optimal proportions, the amount of complement fixed is proportional to the amount of antiserum present.

(11) In mixtures in which delayed and incomplete precipitation is due to relative excess of antigen complement is not fixed.

(12) *It seems probable that complement is fixed during the earliest stages of the aggregation process by which the precipitate is formed. After a visible precipitate has formed very little complement is absorbed. In mixtures which contain a relative excess of antibody precipitation is incomplete and delayed, and the earlier stages occupy sufficient time to allow the complement to be bound.*

(13) To ensure the greatest possible fixation, the complement should be present from the time when antigen is mixed with antibody. If an interval is allowed to elapse before complement is added, very much less fixation takes place.

(14) *The fact that precipitation has been observed without complement fixation, and complement fixation without precipitation, is not sufficient evidence that two separate antibodies exist, for by adding different quantities of antigen to a constant amount of the same antiserum it is possible to demonstrate precipitation without complement fixation or complement fixation without precipitation.*

(15) Complement fixation and precipitation are two methods by which we are enabled to measure the same change which represents the aggregation of the particles of an antiserum by the homologous antigen.

(16) When the complement fixation method is used for the purpose of detecting the presence of antigen it is necessary to use various dilutions of the antiserum. Unless an approximately equivalent amount of antiserum is employed it is always possible that complement fixation may be inhibited by a relative excess either of antigen or of antibody.

(17) In order to make a quantitative determination either of antigen or of antibody it is necessary to titrate various amounts of antigen with various amounts of antibody, for unless antigen and antibody are

present in equivalent proportions the greatest fixation of complement cannot be obtained. After the equivalent proportions have been ascertained the actual amount of complement fixed can be demonstrated by the use of various amounts of guinea-pig serum, of which the complement content has been determined.

(18) The complement fixation method is more convenient than the precipitation method for the purpose of differentiating between nearly allied varieties of bacteria and the sera of nearly allied animals. Complete differentiation can frequently be only obtained by a dilution of the antiserum which is too weak to produce a visible precipitate. Another method of securing differentiation is by the use of various doses of complement.

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Induced Division of Leucocytes and the Genesis of Tumours.¹

By Sir RONALD ROSS, K.C.B., F.R.S.

SCIENTIFIC workers may like to have a brief account of some recent researches which, I think, are likely to be of both theoretical and practical interest. The researches commenced nearly five years ago in a special study of leucocytes by a method devised by my brother, Mr. H. C. Ross, and myself. This consists in placing liquid blood under a coverglass, not as usual upon another surface of glass, but upon a bed of transparent jelly with which various reagents, including stains, have been mixed. The original object of the method was to try to cultivate human leucocytes *in vitro*. The jelly prevents mechanical injury to the blood-cells by pressure, disposes them in a beautifully regular film, and at the same time causes them to be uniformly affected, when living, by the reagents—the whole process being continuously visible under the microscope. At first, careful studies of the rate of absorption of stains by the leucocytes under various chemical conditions of the jelly were made by Mr. Ross; but during this investigation he discovered that atropine and some other alkaloids cause these cells to emit and retract long processes in

¹ Read at the Laboratory Meeting of the Section, held at the Lister Institute on November 7, 1911.

a curious manner. Two years later he found that extract of hæmal gland, extracts of apparently many dead and decomposing tissues, and globin, when mixed with the jelly, force a large proportion of the leucocytes to divide before the eyes. Subsequently he and his assistant, Dr. J. W. Cropper, ascertained by a series of lengthy studies that many of the substances which possess this property (in different degrees) belong to the amidine grouping. They have found also that a second series of substances, though by themselves they cannot produce division of leucocytes, have the power of augmenting very greatly the power of the former group of substances to do so. They give the names *auxetics* and *augmentors* to the two groups respectively. The principal auxetics are extracts of organs—creatine, xanthine, creatinine, guanidine, benzamidine, theobromine, acetamidine, caffeine, theophylline, methylamine, ethylamine, propylamine, &c., and certain aniline dyes. Some of the augmentors are various alkaloids—atropine, choline, cadaverine, neurine, &c.

The technique, though simple, requires considerable care, because exact amounts of salts, auxetics and augmentors must be mixed with the jellies, and the specimens must be kept at the proper temperature from the moment that the blood is drawn from the subject. If a stain, such as polychrome methylene blue, is added the cells become coloured progressively as the division advances. All the varieties of the human leucocytes can be made to divide, but the technique is slightly different for each variety. The proportion of cells affected in a given preparation of blood varies according to perfection of technique up to, say, 80 per cent.; but as death occurs rapidly, especially if stain be used, it usually overtakes a large proportion of them before the division has been completed. After about twenty minutes all the cells die; and by that time the process is complete in only a small percentage. Efforts to keep the cells alive longer upon these medicated jellies, or in solutions of auxetics, have not yet been very successful, and would not be easy. After their death the leucocytes give up again most of their stain, and the jelly preparation rapidly spoils; but a method has been found of making (with some difficulty) permanent specimens of such of the blood as adheres to the coverglass by fixing the whole preparation with osmic acid vapour, and then freezing and picking off the coverglass from the bed of jelly. In such specimens the cells retain the form which they happened to possess at the moment of fixation, and can then be stained when dry.

To watch the same cell passing through the whole process requires

an accurately adjusted warm stage or microscope incubator and considerable patience, because the cell which we happen to select for observation will most probably belong to the majority which die before completion of the division; but partial division can be easily witnessed. If, however, the specimen is incubated for ten minutes, and is then surveyed rapidly from field to field, numbers of the leucocytes caught in all stages of the process can be readily seen. The fixed films just referred to show exactly the same objects, but enable us to examine them repeatedly and at leisure. And in both these cases the dividing forms are so numerous and similar that there can be no question of their being exceptional artefacts or distortions, such as may sometimes simulate almost anything. Division of the mononuclear variety of leucocytes is produced and studied the most easily, but that of the other varieties can with patience be seen quite frequently enough to leave no doubt of the nature of the process.

In films in my possession numerous examples of dividing mononuclears fixed at all stages demonstrate (together with observations of the jelly preparations) the following steps in the process. In a few minutes after the blood is drawn from the subject and mounted, the round so-called nucleus becomes oval and then kidney- or bean-shaped, leading on rapidly to the outline of two circles cutting each other, and lastly touching each other in a "figure of eight." When the process is about half complete, and if the direction of division is parallel to the surface of the jelly or glass, another phenomenon is seen. About four to eight finger-like processes, radiating from the point midway between the centres of the two circles, are protruded or divided off, giving the whole body roughly the appearance of an ant, of which the head and abdomen are simulated by the two spheres, and the legs by the processes just mentioned. Such forms are numerous and characteristic; but, of course, when the direction of division happens to lie at an angle to the surface they are foreshortened, or may be distorted by the pressure of the jelly. As the division proceeds the processes are retracted into each daughter sphere, until the final figure of eight is produced.

If polychrome methylene blue is put in the jelly the cells become coloured progressively as the division advances. At first, after a few minutes, the so-called cytoplasmic, or Altmann's, granules take a purple tinge; then the so-called nucleus becomes a pale blue; and last of all the so-called nucleolus is stained—after which, apparently, the cell dies. As the so-called nucleus proceeds to take the hour-glass and figure of eight forms, strands of coloured substance are seen, especially in the

fixed films, passing between the two daughter spheres; and such connexions are maintained until complete dissociation occurs. Though in the last case it is often, of course, difficult to say after the event whether we are not merely seeing two cells which have fallen accidentally into juxtaposition, yet the previous steps of the process are quite unmistakable. The behaviour of the so-called nucleolus is not easy to follow because, as just noted, it does not stain until the cell dies and further division is checked. On the other hand, the behaviour of the so-called cytoplasmic granules must be described as very curious. In the middle of the division they are found to number about eight (when they can be easily counted) and to lie, each one, at the end of one of the finger-like processes mentioned above; and appearances suggest that half of each granule is distributed to one daughter cell, and the other half to the other daughter cell. No distinct chromosomes are seen at any stage *inside* the so-called nucleus; and there appears to be no sign of astral fibres—though perhaps the finger-like processes may be interpreted as being bunches of these fibres which have not been rendered individually visible by the process of staining employed. On conclusion of the process the so-called cytoplasmic granules appear to be equally distributed between the two daughter cells, and to place themselves on the outer surface of the so-called nucleus of each—that is, in the position in which they were seen in the original parent cell. Apparently asymmetric forms are also frequently seen, but need not be described here.

Such seem to me to be the facts as observed by myself in preparations shown or given to me by Mr. Ross and Dr. Cropper. I will not touch here upon the similar divisions of the so-called polymorphonuclear leucocytes—which have also been already described and figured by Mr. Ross. Nor will I attempt to reconcile the observations with current cytological teaching, even as regards the division of leucocytes. Very probably, different methods of staining may bring them, at least partly, into closer conformity. Though engaged for years in the study of blood I have never seen these forms before; nor, indeed, have I ever seen in any ordinary preparation what could certainly be called a dividing leucocyte. I have been shown bodies claimed to be such, but these are admittedly so rare that they are open to the usual logical fallacies connected with very exceptional observations. The observations here referred to are not open to these fallacies. As I have said, the dividing forms are so numerous and characteristic that we can have no doubt that they really are dividing forms—whatever other observations or theories may be on record. It seems to me, therefore, that we are now compelled

to admit two new facts: (1) that large numbers of human leucocytes can be made to divide *in vitro*; and (2) that this division occurs entirely, or at least specially, in the presence of certain chemical substances.

Such were, in brief, the laboratory experiments; but Mr. Ross suggests that they may already be employed for some tentative generalizations which may be useful as working hypotheses. Subject to correction, I think it was usually held till some years ago that cell proliferation is principally a function of the cell itself, essentially independent of its environment, though often stimulated by temperature, abundance of food, and so on—that is, that most cells divide when mature because it is their nature to do so. In 1900, however, J. Loeb showed that parthogenesis can be induced in the eggs of sea-urchins (*Arbacia*) by the addition of a definite proportion of $MgCl_2$ to sea-water; and since then many workers have studied such phenomena among other animals, while Wassilieff has used hyoseyamine, nicotine, and strychnine for similar researches. The independent observations now recorded would appear to extend cognate principles to body-cells, by showing that the division of leucocytes may be suddenly forced on at a great rate and in a few minutes by the absorption or presence of appropriate chemical agents, and may, perhaps, be inhibited by other chemical agents. Why are the leucocytes never found dividing in normal peripheral blood? Probably (as suggested by Loeb in regard to sea-water) because the auxetics are absent, or because there is some inhibitory substance in the serum (as indicated by some experiments). But why do they proliferate so rapidly at the site of an injury? The auxetics and augmentors are chemical substances, many of which are known to be formed in disintegrating or dead tissues; an injury is, therefore, likely or sure to produce them at the spot where it has occurred; and they will then compel the cells in the neighbourhood to divide as quickly as they compel similar cells to divide *in vitro*. And this hypothesis was supported at once by the simple experiment of placing auxetics upon small spots on the surface of ulcers. Wherever they were put profuse cell proliferation followed, as evident to the naked eye.

The further possible application of the hypothesis to the genesis of at least some kinds of tumours is as follows: It is very probable that many individuals contain in their tissues auxetics and augmentors derived from extensive cell death going on somewhere in the body, as, for instance, in consequence of chronic rheumatism, decaying teeth, old intestinal, mammary and uterine lesions, or even advancing age. In

such persons any new, small internal or external injury might be followed by *overhealing* due to excess of auxetics in the general body plus those formed at the site of injury by the local cell death. Excessive cell proliferation would now occur; but the new cells being over-numerous would perish, would generate more auxetics, and would stimulate in their turn the production of still more new cells. Thus a vicious cycle would be established, and massive tumours such as we see in cancer might be gradually or rapidly built up. We should have here, so to speak, the formation of a kind of internal scab—a process originally intended to be healing, but now perverted into being itself an excitant of its own malignant growth, and of metastatic growths elsewhere. There would be two factors, the general auxetic poisoning (so to speak) and the additional local auxetic poisoning; but it is conceivable that the second factor, if well established, might suffice to maintain the condition by automatically supplying the first factor—thus explaining the frequent success of transplantation of tumours. Conversely, excision may frequently cure by removing the local supply of auxetics. Very probably special kinds of cells require their own special kinds of auxetics and augmentors—possibly obtained from dead cells of their own kind; which may help to explain the numerous varieties of tumours met with.

It is impossible to consider in this brief note the pros and cons of the subject, or the relations which this theory bears to the numerous other excellent studies now being made on cancer, but the following point is of interest. It has been known for some time that warts and epithelioma are exceptionally common among men working with "gasworks tar-pitch," but, curiously enough, not among men working with "blast furnace tar-pitch." In fact, legislation is now proposed to deal with the former, but (expressly) not with the latter. Mr. Ross and Dr. Cropper have recently reported that, on extracts being made of these two substances and mixed with the jellies, the extract from the gasworks tar-pitch was found to be a powerful excitant of leucocyte division, while the extract of the blast furnace tar-pitch was not. Hypothetically, therefore, the constant application of the former to the skin would be likely to have just the effect which it is found to have. Of course, many more researches are required at various points of attack—and some of these are now being carried out under the McFadden Researches at the Lister Institute. The work will probably have many applications. Thus intestinal amœbæ have been shown to grow much more quickly in culture in the presence of some of these auxetics, and extract of dead leucocytes, when injected into men, has been shown to cause a considerable increase of the living cells.

Pathological Section.

November 21, 1911.

Dr. R. T. HEWLETT, President of the Section, in the Chair.

Arterio- and Phlebo-myomatosis.

By S. G. SHATTOCK.

De Arterio- et Phlebo-myomatose.

Hoc nomine laesionem quamdam vasorum adhuc, ut credo, non descriptam, appellare licet.

Observata est laesio in nonnullis vasis fibromatis mollis cujus origo tela pelvis connexiva.

Tumoris vasa, minimis exceptis, tunicae muscularis crassitudinem insignem monstrant.

Non disponuntur fasciculi ad normam ut in vasibus cum hypermyotrophîa affectis, id est, aut transverse aut in longitudinem, sed ita commiscentur ut obscuratur relatio ad vasis axem.

E tunicâ musculari vasis cujusdam, quoad crassitudinem auctâ, oritur tumor lobulatus ex telâ musculari constructus.

Non aegrotabat mulier e renum morbo ad quem incrementum vasorum musculare referri forsitan potuerit.

In toto differt laesio ab illâ a Kussmaul et Maier descriptâ (Periarteriitis nodosa), ubi arteriolarum nodositas tunicae incremento adventitiae sive periarterii causatur, endothelio quoque crassiori, tunicâ musculari autem attenuatâ et disruptâ.

Under the above name I may describe what is, so far as I know, a form of vascular lesion hitherto unrecorded. Although the condition was met with in the vessels of a soft fibroma, it cannot be attributed to anything peculiar in the structure of the latter. The appearances to be described do not bear interpreting—e.g., as due to the distribution of vessels within bundles of muscle occurring in the growth. And the

name, by directing attention to the change, may lead, perhaps, to the recognition of further examples of it.

As to the tumour itself (now in the Museum of the Royal College of Surgeons), it is a large fibroma which grew from the connective tissue of the pelvis by the side of the vagina, and was enucleated by

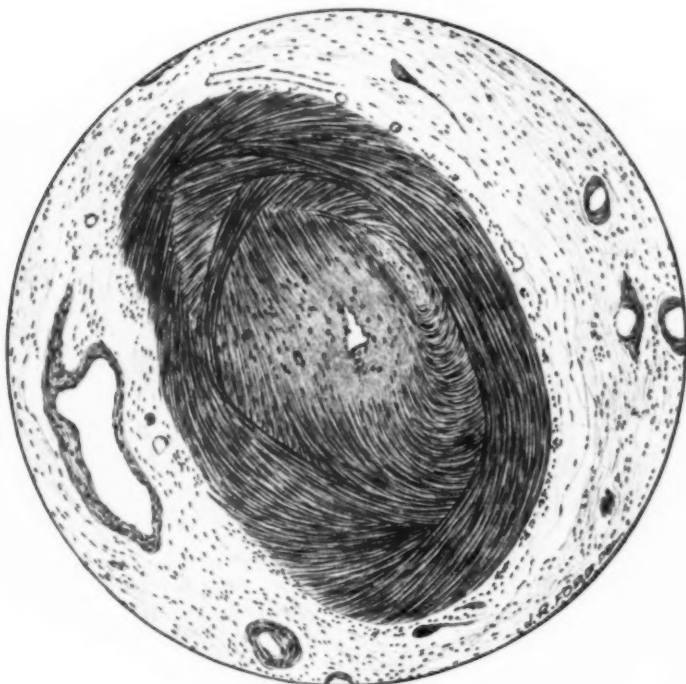


FIG. 1.

Vas transverse sectum e pelvis fibromate, tunicae muscularis incrementum insigne monstrans, fasciculis ut in tumore musculari dispositis. Tunica intima nihil morbidū ostendit.

A transverse section of one of the vessels of the paravaginal fibroma described, showing the remarkable thickening of the muscular wall, the bundles of which no longer preserve the strict normal disposition with respect to the axis of the vessel. The intima is not involved in the thickening; its extent beneath the endothelium may be determined by the oval form of the nuclei of its cells. Obj. $\frac{2}{3}$.

Dr. F. J. McCann. Histologically, it is constructed of a feltwork of delicate fibrils, well provided with flattened corpuscles having large, oval nuclei, the whole structure being typically that of a soft fibroma.

The patient was a single woman, aged 54, who presented a soft, pendulous swelling about the size of a coco-nut, on the left side of the vulva. The uterus was enlarged by the further growth of a fibromyoma, for which supravaginal hysterectomy was performed. During the operation the other tumour was found occupying the left side of the pelvis; the peritoneum was divided, and the growth enucleated as far

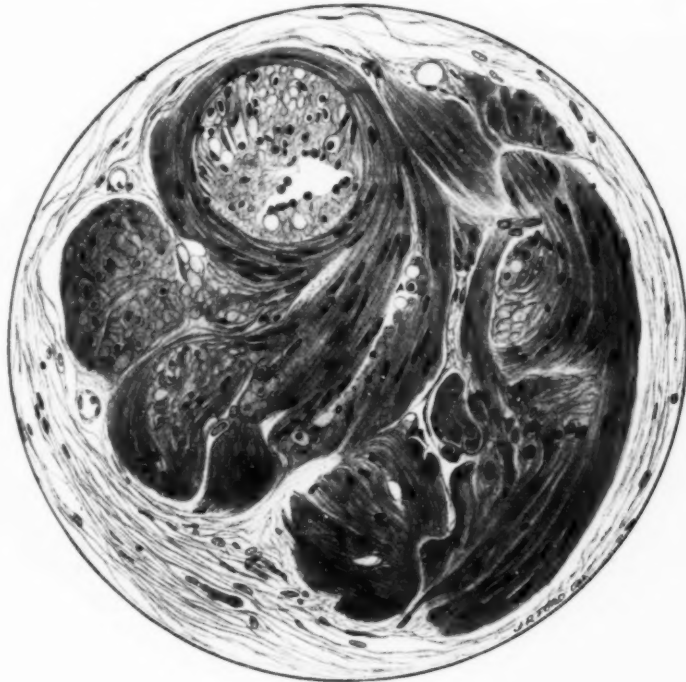


FIG. 2*

Vas transverse sectum ex eodem tumore. E tunica musculari, quoad crassitudinem aucta, oritur tumor lobulatus, ex tela musculari constructus.

A section of another of the vessels of the paravaginal fibroma described. To one side of the overgrown muscular wall there is appended a lobulated mass of muscular tissue having the characters of a myoma; there is but one small lumen in connexion with the whole. The tissue within the circular fibres consists of unstripped muscle longitudinally disposed as in a vein. Obj. $\frac{3}{8}$.

downwards as an opening in the pelvic fascia, through which it passed to become continuous with that projecting on the left side of the vulva. The entire tumour was successfully removed.¹

¹ Dr. F. J. McCann, *Proceedings*, 1912, v (Obstet. Sect.), p. 38.

As studied in the microscopic sections, many of the vessels above the size of the smallest present a remarkable overgrowth of the muscular tissue. In some, the innermost fibres have, in general, a longitudinal disposition; the outer, a circular. In others, however, the bundles of muscle-fibres intersect without such a strict relation to the axis of the vessel, and after the manner of those in a myoma. This will be most readily appreciated by an inspection of the accompanying figure. Further than this, the enlargement may be so disposed as to produce a lowly lobulated or knotty swelling around a portion of the circumference of the vessel.

A measure of the muscular hyperplasia is furnished by the small size of the lumen of the vessels concerned, as compared with their diameter, and this without there being any accompanying infolding of the intima or augmentation in its thickness. Certain of the unaffected vessels, indeed, which present a muscular wall of the normal thickness and of cells regularly disposed, have an absolutely wider lumen than those most thickened from disease, and of a vastly increased diameter.

The *adventitia* is, in some cases, hardly differentiated from the general fibrous tissue of the new growth; in others it is indicated by the circular disposition of the fibre in its immediate vicinity: immediately beyond the limit of the myomatous thickening there are a certain number of capillaries destined for the nutrition of the overgrown muscular tissue.

The *intima* is represented by a single layer of endothelium; and, beneath this, by a thin subendothelial layer of connective tissue in which there lie cells with conspicuous nuclei of the ordinary oval form. No elastic lamina is to be recognized between the intima and the thickened media.

In regard to the relative thinness of the intima, it must be borne in mind that the vessels of which the media is myomatous owe their size to the latter overgrowth, whilst the intima retains its original thickness without partaking in the hyperplasia.

It occasionally seems to happen that two neighbouring vessels with thickened media become fused together by an extension of the muscular overgrowth, but the appearance more probably results from the presence of a loop in the vessel, the lumen of which has been divided in two situations, whilst the periphery of the thickened muscle remains as a bond connecting the two segments. Muscular extensions may stray from the thickened wall for a certain way into the surrounding fibromatous tissue, regardless of the proper limitation and conformation of the vessel. This is to be observed even as regards vessels in which the

muscular thickening is comparatively little advanced, the external limits of the media being very ill defined. That many of the diseased vessels are venules may be concluded from the circumstance that the innermost muscle has a longitudinal disposition, although it is to be remembered that even in normal arteries of the larger size, longitudinal muscle-fibres occur on the inner side of the circular, whilst in the superior mesenteric, splenic, renal, &c., such fibres may lie beyond the circular.

The vessels of the tumour, other than those diseased, comprise tortuous arterioles, wide venous spaces, and a rich supply of capillaries. In some spots the arterioles and small veins are so close as almost to constitute a local plexus. A few nerves of inconsiderable size, and of normal structure, occur here and there in the midst of the fibrous tissue; there is nothing in the least suggestive of a neurofibromatosis.

Slices of the tumour 2 mm. in thickness were kept for a prolonged period in acetic acid in order to render the connective tissue transparent and allow of the thickened vessels being traced, for they are readily discernible by means of the naked eye. After this preparation the surrounding tissue could be teased away and the diseased vessels isolated. The segments of vessels so exposed, one of which happening to lie in the longitudinal direction was 0.5 cm. in length, did not present any nodular enlargement, but were uniformly thickened like nerves in the diffuse form of neurofibromatosis. Although the vessels so affected are comparatively small, it must be remembered that size is not the criterion of tumour formation, but inco-ordinated growth. *Mutatis mutandis*, the same is true of cysts. The largest cysts, for example, in a chronically inflamed breast, merge, in the same organ, into those that are only just visible to the naked eye, and the latter, into those which are microscopic. There are microscopic or microcysts; and, it might be added, there are microscopic tumours. The growth of an adenofibroma of the breast may be traced sometimes, in the multiplication of what are microscopic formations of dense fibrous tissue around individual acini, the pockets of which become extended and magnified by the surrounding growth. Such a stage is figured by Mr. F. T. Paul in the *Transactions of the Pathological Society*,¹ and I can confirm the observation from preparations of my own. I might cite, too, the miliary osteomata of the skin described and figured by Virchow,² as the smallest known examples of this class of new growth; or the minute cutaneous papillomata that are sometimes barely macroscopic.

¹ *Trans. Path. Soc. Lond.*, 1901, lii, p. 30, plate iv, figs. 1, 2, 3, 4.

² "Krankhaften Geschwülste," "Osteomata," Lect. 17.

The muscular overgrowth which I have ventured to describe may be differentiated from such hypertrophy of the media as results simply from increased function, by its inordinate degree and by the fact that the muscle-cells no longer strictly retain the normal circular and longitudinal disposition, but lie in bundles which intersect after the manner of a myoma. Dr. Savill has described and figured marked instances of physiological overgrowth of the media of arteries under the term of "arterial hypermyotrophy," unassociated with intimal or adventitial change,¹ and has pointed out that although an accompaniment of chronic renal disease, the condition may be met with apart from the latter. As he rightly insists, the term "chronic Bright's disease" should be reserved for cases of undoubted renal origin, and should not be applied to those of arterial disease where the kidneys are intact. In this connexion it may be stated that in the case recorded a careful examination of the urine at the time of the operation demonstrated the absence of renal disease.

The heart in all examples of arterial hypermyotrophy, whatever their ætiology, participates in the muscular hypertrophy. The muscular overgrowth affecting the arteries in these circumstances is of a normal histological kind, and presents nothing atypical. Dr. Parkes Weber has, under the title "An Apparent Thickening of Subcutaneous Veins,"² described a "contracted state of the veins (sometimes perhaps merely a result of little blood having at the time to pass through them) in cases where the longitudinal bundles of unstripped muscle-fibres which constitute the inner portion of the tunica media happen to be particularly well developed." Whether there was any actual hyperplasia of the media was undeterminable. He notes, as a histological detail, that occasionally the greater part of the longitudinal muscle is arranged in bundles outside the zone of the circular, only very little lying between the latter zone and the endothelium.

Still less is the condition related to the periarteritis nodosa of Kussmaul and Maier.³ In the latter, although there are local thickenings on the smaller arteries in various parts and organs of the body, the histological characters are altogether different. Von Kahliden,⁴ in his minute description of one such case, remarks that the lesion consists in a proliferation of the endothelium, which breaks through the elastic

¹ *Trans. Path. Soc. Lond.*, 1904, lv, p. 375, figs. 72, 76.

² *Trans. Path. Soc. Lond.*, 1899, l, p. 57.

³ *Deutsch. Arch. f. klin. Med.*, Leipz., 1866, i, p. 484.

⁴ *Beitr. z. path. Anat. u. allg. Pathol.*, Jena, 1894, xv, pp. 581-601.

lamina and muscular coat, the elastic tissue perishing by softening and necrosis; the muscle-fibres last longer, but eventually disappear on the side of the endothelial overgrowth. Accompanying this there is a pronounced round-celled infiltration of the adventitia, which becomes six or ten times thicker than normal; the endothelial proliferation leads to diminution of the lumen. There is no evidence that this inflammation of the periarterium is of syphilitic origin.

A Large Intra-abdominal Hæmatoma formed in an Accessory Spleen.

By S. G. SHATTOCK.

THE vast collection of observations stored in the fifty-eight volumes of the *Transactions of the Pathological Society* has so far exhausted the subject of morbid anatomy that little is to be gained by the simple record of lesions which have been already described. It is nevertheless still true that the *Proceedings of the Royal Society of Medicine* should continue to afford a means of recording whatever is either new or very rare in morbid anatomy, even of the grosser macroscopic kind.

The following specimen may be described for these reasons, and more particularly since it was sent to the Museum of the Royal College of Surgeons, from the Pathological Department at Oxford as something altogether unique and inexplicable. It is a spleen to the concave side of which there is attached an oval cyst 12 cm. ($4\frac{3}{4}$ in.) by 8.5 cm. ($3\frac{3}{4}$ in.) in its chief diameters. The wall of the cyst is of dense homogeneous connective tissue, and averages 2 mm. in thickness; and it is prolonged over that part of the cyst which lies against, and which is incorporated with, the proper splenic capsule. The capsule of the spleen itself is not thickened; the length of the viscus is 10 cm. (4 in.), and its structure is normal.

The contents of the cyst consist of a finely shaggy, pale reddish-brown substance which forms a lining about 0.5 cm. ($\frac{1}{4}$ in.) in thickness, from which a few coarse septa pass, so as to subdivide the cavity into extensive loculi somewhat like those of a hydronephrotic kidney. The spaces so formed are lined, like the inner surface of the peripheral layer of spongy substance, with delicate films of fibrin. A piece of the omentum, which is adherent to the cyst, has been removed with it.

The parts were excised by Mr. Dodds-Parker at the Radcliffe Infirmary, Oxford, from a married woman, aged 35, the mother of eight children. For twelve months before admission she had suffered from aching pain in the left lumbar region. At the first onset the pain was so severe that it "doubled her up," and it did not quite disappear for a week; there was no vomiting. She felt a lump in the abdomen ten months before admission. The patient, when seen, was somewhat wasted but without any sign of organic disease except that palpable in the abdomen.

Examination disclosed a soft, fluctuating swelling the size of a coco-nut, in the left iliac region. The swelling was freely movable into every region of the abdomen; no pedicle could be made out connecting it either with the uterus or the ovary; on one of its sides there was a notch. Both kidneys were palpable. The parts were easily removed by operation, the splenic artery having been ligatured. Recovery was uninterrupted.

Histologically, the thick wall of the cyst presents the usual structure of all such capsular thickenings, and consists of dense lamelliform fibrous tissue of the corneal type—of hyaline-looking, parallel lamellæ, furnished with flattened intervening cells in linear series. The material within consists of a meshwork of ill-stained, finely granular substance. Mingled with this are patches of a fibrinous feltwork, in the meshes of which decolorized red blood-cells are entangled. The granular material, moreover, is in places very thickly strewn with decolorized red cells; and the definite strands in which this is in parts disposed are strongly suggestive of splenic substance ploughed up by hæmorrhage.

In sections including the subcapsular portion of the material, a certain number of macrophagocytes, holding deep brownish-black granules of blood pigment, occur about the débris; some of these cells are of particularly large size, or hypertrophic; and some contain two or even three nuclei; the cytoplasm of some is coarsely vacuolated. Both macroscopically and microscopically, therefore, it will appear that the findings are those of a simple hæmatoma; there is no indication of the hæmorrhage having occurred into any form of new growth, and the lesion may be fully explained as having had its source in an accessory spleen. Its close connexion with a perfectly normal spleen is, on this supposition, rendered intelligible; and equally so are its size and the character of its capsule; the view is, moreover, congruous with the history of sudden pain twelve months previously, and the recognition of a swelling in the abdomen two months later.

Pathological Section.

January 16, 1912.

Dr. R. T. HEWLETT, President of the Section, in the Chair.

Two Cases of Amaurotic Idiocy, or Tay-Sachs Disease.

By J. TURNER.

THE two following cases of Tay-Sachs disease are interesting from several points of view, the chief being that one is, so far as I know, the first yet published, out of upwards of a hundred reported, which occurred in a child not of Jewish extraction.

CASE I.

Emily W., female, aged 13. Admitted May 4, 1897. Family history: Father, a sober man, killed. He belonged to the Christian Israelites in Islington. Her brother, now aged 28, and apparently healthy and sane, gives me this information and adds, "I do not think he was of Jewish persuasion; I do not think I am Jewish." Her mother, a nervous, irritable woman, living in 1897, but since has died. Mother's mother died, aged 65, of paralytic fits, of which she had four or five. Patient is the youngest of twelve. The first ten died either at birth or were born dead, or lived only seven months; the eleventh a boy living, aged 14.

The patient was operated on in 1891, and an "abscess taken out of her brain"; before the operation her left eyeball "protruded like a bladder." Since then she has had necrosed bone removed from the operation wound several times. She formerly spoke quite well and without repetition. Her first fit was in 1895. Sometimes she has as many as seven in a day.

On admission she was 49½ in. high, and weighed 54 lb. She had a large cicatrix over the left eye, and a scar on the lower ramus of the jaw on the left side. Left knee was enlarged, but the movements free. She was fairly nourished and of pleasing, lively expression. Her gait was slow and with a tendency to turn round and round. Complexion clear. Palate shallow and with thick edges. Teeth small but in good condition; separated from one another. Pupils equal; they react to light. Marked amblyopia with contraction of the fields of vision; can apparently only see objects immediately in front of her; avoids large obstacles, but ran her face up against my stethoscope when it was held near her face. Appears to see better on some days than on others. No mention of nystagmus. Knee-jerks: Left normal, right brisk. Although her gait is clumsy she is a restless little creature. Nurses an old doll and seems much attached to it, hushes it, &c., and howls when it is taken away from her.

Speech: Utters her words rapidly and never more than two or three in the form of a sentence. Nearly always repeats her words—e.g., "Can I, out there—look, look—dicky, dicky." Says "thank you" when given anything. I cannot get her to name things, and only very rarely to repeat them after me. Copied me when I said "me-ow" and "bow-wow" and when I whistled. When I say "one" and ask her to repeat after me, she says "two," and "five" when I say "three," and "seven" when I say "six." Understands what is said to her, but very difficult to fix her attention. Often noisy at night, calling out "oi-oi," and laughing. Slaps my hand and says "cry," and when I pretend to do so she laughs. When offended exclaims "stinks-stinks."

Sensation: Feels light prick on face or hands, puts her hand to the part pricked and slaps me. Ejaculates "cold, cold," when she puts her hands in cold water.

General character: An elfish little creature, very passionate and self-willed, but lovable and attractive.

Fits: The following is a record of the fits noted during her residence in the asylum: May 5, 1897, at 6.20 a.m. May 11, 1897, at 7.45 a.m., left arm, leg and eye twitched; left eye open, right eye shut. Whilst in the fit she tore at the place on her forehead with left hand. Fit said to have lasted ten minutes. May 19, 1897, 8.30 a.m. I saw her immediately after; her pupils were widely dilated, the left the larger. Conjunctival reflexes absent. I was told that during the fit the right leg was bent up and stiff. She did not pass urine. The fit only lasted a minute. 11.30 a.m.: Had another fit, during which she lay on her

back with head turned to the left, eyes to the left, left arm extended from body, and showing clonic spasm; right arm bent across the chest and still; clonic spasm of the left leg; frothing at the mouth. The attack lasted two minutes, and afterwards she kept tapping on the floor with her right fist; the left arm and leg were flaccid and ? paralysed. Moved the head over to the right; pupils widely dilated. There is mention of a fit on the morning of the 27th of this month, and one on June 2, at 3.30 p.m., in which the *right* side was convulsed. She had occasional fits until her death, but they are not described. She was very fretful after the attacks.

On April 10 she fractured the shaft of the left femur. On April 27, sore over the sacrum developed, and on April 29 she died; temperature, 103° F. Her temperature was taken twice daily from May 18 to June 1, 1897, and was generally up to 99.2° F. in the evening.

Autopsy (a few hours after death).

Depression over the left orbit; left knee bent and ankylosed; lower end of the left femur enlarged, and the bone was soft; soft callus uniting the fracture at the junction of the middle and lower thirds.

Head: Skull thin and not dense; membrane only over a round patch the size of a florin in the left frontal region, just over the orbit (trephine hole).

Dura dense; blood-vessels healthy; circle of Willis natural; pia-arachnoid thin, somewhat œdematous, stripped easily; excess of clear fluid beneath the dura. Marked atrophy of the convolutions and the brain was very firm, especially the cornua Ammonis. Cortex thin and pale, ventricles not dilated. Stem firm, small; floor smooth; cerebellum firm. Encephalon, 862 gm.

Thorax: Adhesions of pleura on the right side at the apex and posteriorly. Right lung tough, congested throughout and solid in the lower part; left crepitant. No enlarged glands. Heart small (135 gm.); valves healthy, cavities full of fluid blood, wall of the left ventricle thick and firm.

Abdomen: Glands of mesentery enlarged, soft. Liver (847 gm.) mottled on section; no gall-stones. Spleen (59 gm.) soft. Intestines healthy. Right kidney healthy (101 gm.), capsule stripped well, cortex wide; left (98 gm.), capsule stripped well, cortex narrow, colour pale.

Films of ascending frontal convolution stained in methylene blue: Betz cells fragile, *small* and deeply stained, with large excess of pigment. Dendrites generally fractured by the pressure of making the film. They

stain dull blue and show no tigroid. Cytoplasm intensely stained and very little tigroid can be made out. Apex pale, but shows no tigroid. Nucleus generally central and shows in many cases a paler zone around it. The very great majority of the nerve-cells of all layers are globular and, by artificial light, appear of a pinkish colour with a blue nucleus. The apices are attenuated. The Purkinje cells are very large and globular, and the cytoplasm appears of a reddish tinge, with at one part a small, generally oval area of a bluish tinge, with indistinct tigroid in it. The nucleus in some cells is dimly visible; the dendrites are bulky and present varicosities, no tigroid visible in them. Only the ascending frontal convolutions and the cerebellum were examined microscopically. In view of the very exhaustive accounts published by Gordon Holmes, Mott and others, it is not necessary to give a detailed account of all the pathological appearances. It is enough to state that they were pathognomonic of amaurotic family idiocy or Tay-Sachs disease, and they are so distinctive that it is impossible to mistake them.

Ascending frontal convolution: The chief points to be mentioned are—(1) That in sections stained by specific glia stains (Beneke's) there is very little appearance of glia proliferation. There was a very thin sclerosed rim to the first layer and a few small glia cells in the white matter. (2) There was a very considerable infiltration of lymphocytes in the pia-arachnoid and in the peri-adventitial spaces of the cortical vessels. (3) Cells: With Van Gieson stain the pigmented part stains very pale green and is granular, the cytoplasm around the nucleus is of a reddish colour. The nucleus is pale red and granular with a green rim, and the nucleolus also pale red with a sharply defined green rim. Over the cell is a dark green covering, somewhat reticulated in places (?Golgi nets). As in the film preparations so in sections, the small cells of the second layer are much less affected.

CASE II.

B. N., male, aged 5. Admitted November 22, 1905. The boy's father, who has a small farm in Essex, informs me that neither he, the father, nor his wife are Jewish, nor, so far as he knows, are there any Jewish ancestors on either side. The father is an Essex man.

The patient was undeveloped, weighed only 39½ lb., unable to stand or talk; had a large umbilical hernia and no thumbs—a very small wart on the left hand seemed to be the only representative of a thumb. His knee-jerks are exaggerated, his plantar reflexes of the flexor type. Palate wide, teeth small and peglike; his tongue lolls out of his

mouth and he slobbers: he can swallow fairly well. He makes a clicking noise with his tongue, but cannot articulate. He is helpless, but gives no more trouble than would an infant. Stated not to be an epileptic. Beyond the statement that he was quite unobservant, there is no mention made of his sight. In the condition he was in it would obviously be difficult to test. On January 7 there is a note that during the past week he has had twitchings of face and eyes. He now lies on his back with flaccid limbs and absence of conjunctival reflexes. There is no plantar response, and no reaction to pricking in legs or arms, but when pricked on the cheek he draws up the muscles of the stimulated side, and the same with the brow. He breathes regularly and slowly, occasionally whimpers, and draws up his arms and holds them suspended for a short time. Slight vertical nystagmus; can swallow. Temperature normal; feet cold. On January 8, 1906, he died.

Autopsy (four and half hours later).

Poorly nourished; no bedsores. Spinal curvature in the lower dorsal region.

Dura mater very adherent to the skull, especially on the right side; blood-vessels healthy. A firm, white subdural membrane, $\frac{1}{8}$ in. thick, covered the cerebrum on both sides, and lined the floor of the middle and posterior fossæ; there was a great excess of blood-stained fluid. The pia-arachnoid was very thick and milky over the vertex, and stripped readily; great excess of sub-arachnoidal fluid. The gyri were very shrunken, tough, and discoloured brown in the right superior parietal lobe. The cortex was narrow and dark-coloured. The lateral ventricles were dilated and filled with fluid. Basal ganglia very tough; pons very tough; ependyma smooth; cerebellum firm. Spinal cord very firm, its central canal for a short stretch in the cervical region was dilated, and measured 3.5 mm. by 1.75 mm.

Weights: Encephalon, 993 grm.; spinal cord, 25 grm.

Thorax: There was a pneumonic patch in the left lung, no pleural adhesions. The heart was very small (70 grm.), the mitral cusps thick and puckered, the aorta healthy.

Abdomen: Liver (720 grm.) was tough, and on section showed pale patches. Gall-bladder full of bile, no stones.

Spleen (95 grm.) tough; kidneys pale, capsules stripped well, weighed together 120 grm.

Portions of the ascending frontal convolution, the cornua Ammonis,

the thalamus (through the anterior tubercle), and the cerebellum were stained by my pseudo-vital method. In the ascending frontal region the striation was good, there was no obvious paucity of nerve-cells.

The method used differentiates two kinds of nerve-cells in grey matter: (1) The ganglion or pyramidal system, which represents the orientated cells of all the layers, and (2) a series of darkly stained, generally small cells found scattered throughout all the layers. Of these two classes the ganglion cells were chiefly affected, and the Betz and third layer cells most of all. The small cells of the second layer were those least affected. Many of the darkly stained or intercalary nerve-cells appeared fairly intact, and this condition is of interest, as we note a very large number of beaded intercellular neurofibrils in the matrix of the grey matter, and it is from the intercalary cells that, in the opinion of the writer, these beaded neurofibrils are derived. The amount of gliosis observed in the section was insignificant.

Cornu Ammonis: The ganglion cells of the stratum pyramidalum are affected as deeply and as universally as those of the ascending frontal. The cells of the stratum granulosum are much less affected, apparently not more than one in ten. Many subcortical nerve-cells are seen, and they are all affected in the same way as the cortical cells. In one part of the white matter, adjacent to the stratum granulosum, there is a small patch of glia cells, but elsewhere none are visible.

Thalamus: In the thalamic section every one of the ganglionic nerve-cells is deeply affected, probably to a greater extent even than the cortical cells.

Dr. Mott, in his article,¹ figures a hexagonally reticulated appearance of the nerve-cell, which he describes as an intracellular network. A similar hexagonal structure is well shown in my sections, especially in the thalamus. I am inclined to think that it represents the meshes of the Golgi net enveloping the cell-body, and not an intracellular structure. This view is strengthened by the appearance often to be observed in the swollen dendrites, more especially of the Purkinje cells, where, at the centre of the swelling—i.e., at the most prominent part—the meshwork is absent, whilst it is well seen over the less swollen parts—an appearance suggesting that the plane of the section has passed through the most convex portion of the dendrite, and denuded this part of its netlike envelope. No intercalary cells could be identified in this region. There was no increase of neuroglia, the peri-adventitial spaces contained a considerable number of lymphocytes.

¹ *Proceedings*, 1911, iv, pp. 147-98.

Cerebellum: There was great fibroid thickening of the meninges. All the Purkinje cells show the changes, but the final terminal dendrites are abundantly covered with *thorns*. Very many, probably the majority, of the intercalary cells of the molecular layer are affected. The neuroglial fibres of Bergmann are visible in places, and there are some glia cells seen in the white matter. The granules show no alteration.

Spinal cord (Nissl-stained sections): The anterior horn cells are large and numerous. All show the change, but to a less degree than the brain cells—i.e., around the nucleus is a larger region containing fairly normal tigroid. The nucleus is rather small and angular, but clear. No gliosis noted.

In Weigert-Pal preparations the swollen (pigmented) part of the cell-body shows coarse brown granules, and in those cells where the change is more pronounced these granules become much smaller, paler and sparser, and frequently in the centre of the mass there is a quite colourless, structureless area. This advanced stage is much more general in the cervical than in the lumbar region. In Marchi preparations the pigment granules are not darkly stained, and often the centre of the pigment region is paler than the cytoplasm.

Central canal: In the cervical region, for a short tract, this canal was enormously distended, so that it measured 3.5 mm. on transverse section; it was lined throughout by cylindrical epithelium. In the lumbar region the canal was small. There is well-marked old degeneration of the pyramidal tracts, most marked in the cervical region.

The histological features of Tay-Sachs disease are pathognomonic, so that although in neither of my cases was there evidence of the disease affecting more than one member of the family, and in neither were the eyes examined for the characteristic cherry-red spot on the macula lutea, we may have no hesitation in accepting them as instances of this disease on the histological findings alone.

So far, according to the recent article of Carlyll and Mott in the *Proceedings of the Royal Society of Medicine*, March, 1911,¹ although there is a record of over a hundred cases, no genuine instance of the disease has been recorded in any but a Jewish child. At first I thought both my cases were exceptions to this rule, but inquiries elicited the information that the father of Case I was a Christian Israelite, and, in spite of my informant's (the patient's brother) unwillingness to admit

¹ *Proceedings*, 1911, iv, pp. 147-98.

his Hebrew extraction, I think we must regard this case as no exception to the rule. The other, however, occurred in the son of an Essex man who assures me that neither he, his wife, nor any of their forbears, so far as he knows, have or have had any Jewish blood in them. So that we may fairly certainly conclude that Case II is an exception to the hitherto unbroken rule, that only Jewish children suffer from the disease. This fact alone would amply justify me in publishing the case, but there are also other points of interest to be noted in both, in respect to the age of the patients, the pathological appearances as seen by special staining, and the ætiology of the disease.

As regards the age, both were far beyond the limit generally assigned to this disease. Carlyll, in the paper just quoted, states that it is justifiable to tell parents that children with this affection will not reach the age of 3. My first case was 14 when she died, from an inter-current complaint; my second was over 5.

Mott takes exception to the name of "idiocy" applied to the disease, but his objections lose their force when this name is applied only to cerebropathic states in infants, either before, at, or shortly after birth. This is the sense in which many, including the writer, now use the term. So that instead of idiocy being only a severe form of imbecility, it has no connexion with imbecility and lies at the opposite extreme in the classification of insanity, that is to say, among the traumatic (using this term in its widest sense) insanities. And the very lack of developmental defects, on which Mott rests his objections to the term "idiocy," becomes strong evidence why the disease, from the cerebropathic point of view, should be termed idiocy. However, it should be noted that Case II did show certain features which might be looked upon as stigmata of degeneration—to wit, absence of thumbs and dilatation of the central canal of the cord.

Gliosis, using the term as connoting an overgrowth of neuroglia in contradistinction to other glia cells (mesoglia), is evidently not an essential feature of the disease. It was present to only a slight pathological extent in both my cases and was absent in all the cases described by Gordon Holmes,¹ and indeed it has, with very few exceptions, been absent or inconsiderable in all the cases so far reported.

I look upon the meshlike fragments seen on the swollen cells and their dendrites as Golgi nets, and I have produced evidence² that these nets are a derivative from the mesoglia cells which occupy the peri-

¹ *Brain*, 1906, xxix, pp. 180-208.

² *Brain*, 1904, xxvii, pp. 64-89; *Rev. Neur. and Psych.*, Edinb., 1905, iii, p. 773.

cellular space. If the accumulation of nuclei in these spaces are nuclei of mesoglia cells, then an increase of this tissue is, if not an essential, at all events a very common or constant feature of the disease. The abundance of beaded neurofibrils in the cortex in Case II is of interest, considering the very extensive condition of alteration in the ganglion cells. This may to some extent be accounted for by the lesser participation apparently of the intercalary or darkly stained cells in the diseased process, if, as the writer believes, these beaded neurofibrils are given off by these cells.

A word as to the aetiology. Can syphilis be so certainly excluded from the causation as Carlyll would have us believe? In both my cases there were points suggestive of syphilis. In Case I the mother gave birth to ten children, who were either still-born or only lived a few months, before giving birth to Emily. The character of the patient's bone lesions was suggestive of syphilis, as also the proliferation of lymphocytes in the peri-adventitial spaces of the vessels of the brain cortex. In Case II the small peglike teeth and the peri-adventitial proliferation around the cortical thalamic and caudal vessels. Then, further, Gordon Holmes in the same number of the *Proceedings of the Royal Society of Medicine*¹ already quoted from, records a case of amaurotic idiocy, where also the peri-adventitial cellular infiltration was, as the author remarks, suggestive of congenital syphilis, and this case was the brother of one of Carlyll's cases. Mott states that he has examined all the tissues of the body in several cases, and could not find any glandular lesion. This is a somewhat gigantic task, and it is quite possible that, even granting the lesion to be visible to the microscope, it may have escaped notice. So that the suggestion made by Gordon,² that the disease owes its origin to a failure of metabolism, the result of some gland lesion or anomaly, is not one to be hastily discarded.

Mott hypothesizes that the changes found in the nerve-cells are due to a failure in the nuclear material to build up the nucleo-protein Nissl substance out of lipid substances contained in the cytoplasm, which have first to be decomposed by a nuclear ferment. The pigment, he states, is a fatty substance of the nature of a lipid, as it stains by all the methods which stain the myelin sheath, and with Scharlach red—a specific fat stain—it colours more or less intensely in proportion to the degree of swelling and morphological change. He notes that it stains *unsatisfactorily* with Marchi's stain. In my preparations stained

¹ *Proceedings*, 1911, iv, pp. 199-204.

² *New York Med. Journ.*, 1907, lxxxv, p. 294.

by osmic acid after bichromate hardening, I found an entire failure of the pigment to stain with osmic acid; in parts it was even lighter than the cytoplasm. Mott attempts to explain this failure to stain, or partial failure (in his cases), by assuming that the process of decomposition of the lipid into glycerophosphoric and oleic acids is incomplete. Mott's hypothesis is ingenious, though how far his efforts to account for the unsatisfactory staining of the pigment with Marchi in his cases are convincing is a moot point. I should like to accept them, but find it difficult to believe that if, as he supposes, there is a process of decomposition going on, at least in places it would not have arrived at the stage when the pigment would be in a condition to react to osmic acid in the way characteristic of non-phosphorized fats. But granting his explanation to be substantially correct, it is still most compatible with a failure in metabolism due to some gland deficiency or anomaly, and if so, then amaurotic idiocy must be ranged alongside the idiocy produced by defective thyroid secretion, and perhaps, like this, it will eventually yield, in part at least, to therapeutic measures.

An Unusual Organism (*Micrococcus zymogenes*) in a Case of Malignant Endocarditis.

By J. A. BRAXTON HICKS.

My excuse for bringing this paper before you is that the isolation of the organism found in this case of ulcerative endocarditis has not been before recorded in this country, as far as I can ascertain from a perusal of the literature. The organism, the cultural characteristics of which I shall describe later on, was first isolated by two Americans, MacCallum and Hastings [4], in 1899, from two cases of ulcerative endocarditis; and they, having thoroughly worked out its cultural peculiarities, named it *Micrococcus zymogenes*, because of the liquefying properties of the products of the organism even after all bacteria had been removed by filtration.

The few subsequent recorded instances of the isolation of this organism have been made by American writers, namely, Harris and Longcope [2], who isolated it from a series of four autopsies where it appeared to be a secondary infection, and once from the contents of

a cesspool, and Birge [1], who found it in the larynx of crows. I cannot find any mention of it in the French and German literature except as references to the American cases, and the only text-book of bacteriology in which I have been able to find any reference to it is that written by our President [3]. I may, however, have overlooked its record, and should be glad to be corrected, if possible, on this point.

CLINICAL HISTORY.

The clinical history of the case was briefly as follows: Mrs. M. M., aged 40, a patient of Dr. Foott, of Enfield, was admitted into Westminster Hospital in March, 1911, under the care of Dr. de Havilland Hall. There was no previous history of any importance, but she said that for the past twelve months she had felt "run down." In September, 1910, she had had a "poisoned finger," which, however, soon got well. Shortly after the finger got well she had an attack of sudden pain in the left side and down the left leg. In October, 1910, she was seized with sudden pain in the right calf, and, later on, by severe pain in the head and left arm. These symptoms disappeared and she improved for a while, when she was seized with sudden pain and swelling of the left foot which compelled her to take to her bed, and where she remained till admission to the hospital in March, 1911. On admission to hospital her physical signs were those of a much enlarged heart (pulsation over third, fourth, fifth, and sixth interspaces and apex-beat 2 in. outside nipple-line), with a feeble apical thrill, faint presystolic and loud systolic apical bruits, with accentuation and reduplication of the pulmonary second sound. No pulsation could be found in the left radial or ulnar arteries, and there was great tenderness over the lower third of the left humerus. The fingers showed clubbing; there was no œdema of the feet. Temperature varied between 98° F. to 100° F. or 101° F. Three weeks after admission the spleen was found to be palpable 3 in. below the left costal margin, and a month after admission there was sudden pain in the left loin with hæmaturia. In April I was asked to make a blood cultivation, and for that purpose took 10 c.c. of blood from the left median basilic vein, using "Hebb's syringe" and the strictest aseptic precautions. The blood thus obtained was inoculated into three broth flasks and from each of these flasks was isolated an organism which subsequently proved to be *Micrococcus zymogenes*. A vaccine was made in the Bacterio-therapeutic Department by Dr. Carmalt Jones, but, owing to the profound disturbance of the patient

which followed even a very small dose of this vaccine, it was discontinued. The patient left hospital in May and died of cerebral embolism in July. No post-mortem was obtained. I am much indebted to Dr. de Havilland Hall and Dr. Foott for their clinical notes on the case.

DESCRIPTION OF THE ORGANISM ISOLATED.

Morphology: The organism is a Gram-positive micrococcus which differs slightly in its arrangement, according to the medium on which it is grown. From solid media it is obtained in film preparations singly, in pairs and in masses and occasionally in chains, though chains are commoner in liquid media and are sometimes quite long. It stains well with aniline dyes and is non-motile.

Agar: On agar it grows well as a thin, slightly elevated, moist, greyish growth somewhat difficult to see by reflected light but readily seen by transmitted light. Occasionally small isolated colonies occur, or the growth may be composed of many coarse streptococcal-like colonies.

Broth: In broth the growth makes the medium cloudy during the first twenty-four hours. After a few days the organisms settle down and leave the supernatant fluid clear. No indol is produced.

Sugar litmus media: Acid, but no gas, was produced in glucose, lactose, saccharose, mannite, maltose.

Gelatine: In gelatine stabs a white, opaque growth occurs along the stab, and, after thirty-six hours, cupping of the medium occurs and liquefaction proceeds slowly downwards.

Potato: On potato a feeble growth occurs, but not always constantly at each subculture.

Blood serum (horse): On this medium the growth was feeble and no liquefaction occurs.

Milk: It is in this medium that we obtain the characteristic reactions of this organism. In litmus milk, the milk rapidly becomes decolorized, and, within twenty-four hours, firmly clotted with a bluish-red layer at the top. The upper layer of this clot now gradually liquefies into turbid fluid which soon takes on a reddish tint above, remaining yellowish below. This softening and liquefaction, with the acquisition of a red tint, progresses day by day, the layer of the red fluid increasing in depth and the remains of the coagulum forming a precipitate at the bottom of the tube. Finally the entire coagulum is liquefied and the precipitate stained deeply red, so that we have a red-

stained precipitate at the bottom of the tube and reddish, clear supernatant fluid above.

Vitality: The organism is a hardy one and survives in subcultures for some time. I have kept mine alive easily by monthly subcultures for ten months.

Pathogenicity: White mice survived the injection of 2 c.c. in the dorsal region. They showed signs of being unfit on the third day after infection, which increased on fourth day. On the sixth day they started to recover and eventually got quite well. Guinea-pigs showed no ill-effects from large intraperitoneal injections.

COMPARISON WITH THE PREVIOUSLY RECORDED ORGANISMS.

The organism I have described is identical with that noted by the previously mentioned American authors. MacCallum and Hastings sometimes obtained a brown growth on potato, which I have not done in my case, but these authors also note that it sometimes fails to grow on potato as I have done. MacCallum and Hastings found that blood serum was slowly liquefied, which I have not been able to confirm, but they used human serum (solidified) which I have not had the opportunity of trying.

With regard to the pathogenicity for animals, this, again, has been found variable by the American recorders. Thus Birge found it non-pathogenic and Harris and Longcope found it non-pathogenic in two out of five cases. Harris and Longcope also found that, grown on media for a short time, it quickly loses its pathogenicity for white mice, which MacCallum and Hastings had found to be the most susceptible to it of the laboratory animals. This possibly explains the lack of pathogenicity in my case, as I did not perform animal experiments till after several subcultures.

Apart from the variabilities I have mentioned, and which have already been noted by previous recorders, the organism is identical with that named *Micrococcus zymogenes* by MacCallum and Hastings.

RELATION OF MICROCOCCUS ZYMOGENES TO THE ULCERATIVE ENDOCARDITIS.

I am not in a position to state what the causal relationship of the organism *Micrococcus zymogenes* is to the ulcerative endocarditis in this case. It is probable that it is merely a terminal infection, as is the

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case with many of the organisms of the streptococcus family in other cases of ulcerative endocarditis. I am sorry that an agglutination reaction could not have been successfully carried out, but the tendency of the organism to cling together in clusters rendered results of very little value. Complement-fixation experiments with the coccal group of bacteria are not, in my experience, of great value.

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Typical examples of the cultivations on various media were shown, including a series showing the typical "milk reaction."

Pathological Section.

February 20, 1912.

Mr. S. G. SHATTOCK in the Chair.

The Relation of Salvarsan Fever to other Forms of Injection Fever.

By EDWARD C. HORT and W. J. PENFOLD.

WHEN injections of salvarsan in saline began to be widely employed, it was soon found that fever might ensue. Although many theories have been advanced to account for this accident none of them will explain all the facts. On the contrary, we find that salvarsan fever is so closely allied to other forms of injection fever that we thought that this relationship might afford an interesting subject for discussion. In order, however, to make clear the points we wish to make a slight historical digression is necessary.

In 1906 it was shown by Kottmann [4] that injection of saline into man might give rise to fever, and this was confirmed by Schaps [6] in 1907. Since then many workers have shown that injection of animals with saline may have the same effect. Salt fever, therefore, as it was called, became established in the literature, and numerous theories sprang up as to its meaning, all based on the belief that salt was the active pyrogenetic agent. Under this heading also really belongs the fever that may follow the injection of saline in intravenous anaesthesia, surgical shock, hæmorrhage, cholera, and so forth, though often the condition demanding treatment has been held responsible for the fever. Fever after injection of sea-water is a recent addition to this group. In 1910 one of us found [1] that the injection of animals with sterile water also caused fever, which therefore came to be known as water fever. In the belief that the water was absolutely pure this worker maintained that water fever was an auto-intoxication, and in August, 1911, suggested [2] that salt fever and salvarsan fever were in reality only different forms of water fever. In the last few years it had also

been found that the injection of certain other substances, such as sugar or tissue extracts in water or saline, would give rise to fever. Accordingly carbohydrate fever, tissue fever, protein fever, ferment fever, and so forth, all took their place in the literature as definite clinical types. In each case the substance injected was credited with specific pyrogenetic properties. And finally came salvarsan fever. Here, then, we have all these types—water fever, salt fever, sugar fever, ferment fever, tissue fever, anaesthesia fever, surgical fever, sea-water fever, and salvarsan fever, each apparently the result of different causes.

In December, 1911, we showed [3], so far as we know for the first time, that there is good reason to believe that some of these different

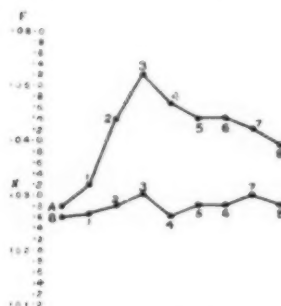


CHART 1.

Chart 1.—**A**, Rabbit, 2,083 gm. injected intravenously with water containing fever toxin and from which 73,000 organisms per cubic centimetre have been removed by centrifuge. Injection ratio 1 in 211. **B**, Rabbit, 2,983 gm. injected with deposit in pure water of 6,000,000 organisms thrown down from above water after thirty minutes in centrifuge tubes. Quantity of water injected 0.50 c.c. Observations every 30 minutes.

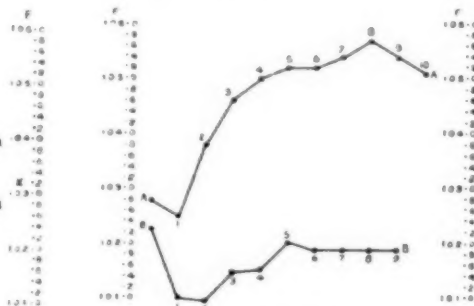


CHART 2.

Chart 2.—**A**, Rabbit, 2,500 gm. injected intravenously with c. 40 million heated *Bacillus typhosus* organisms. **B**, Rabbit, 2,448 gm. injected intravenously with c. 50 million saline-grown organisms after heating and centrifuging from saline injection of which in ratio 1 in 50 produced no fever. Interval between observations 30 minutes.

types of fever are due to a common cause. Our experiments leading to this result were suggested by a theory advanced by Weichselmann [7] that salvarsan fever is due to gross infection, demonstrable at the time of injection, of the solutions of salt and salvarsan. Weichselmann's theory as to the cause of salvarsan fever was subsequently endorsed by McIntosh, Fildes, and Dearden, working in Dr. Bulloch's laboratory at the London Hospital, as a result of independent observation. The theory at first sight seemed to afford a clear explanation of salvarsan

fever, because the liquids examined, either before or after the addition of salt, were reported to contain large numbers of organisms. Moreover, if saline made with freshly distilled water were used, it was found that salvarsan fever did not occur. This was in one instance [5] also true after injection of a filtered sample of sterilized saline made with water that contained before filtration large numbers of organisms, and the apparent effect of the filter in preventing fever was therefore used as an argument that salvarsan fever and salt fever are necessarily due to the actual presence of micro-organisms. No control experiments, however, were cited by these observers to show that organisms grown in pure saline are, if injected immediately after heating, in actual fact themselves capable of producing fever. And from the evidence adduced [5] in support of the statement that filtration will render toxic saline atoxic, it is not clear whether the toxicity, in terms of fever, of the unfiltered

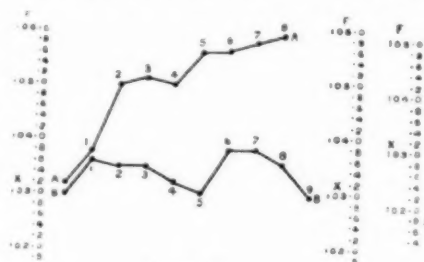


CHART 3.

Chart 3.—**A**, Rabbit, 2,324 gm. injected intravenously with 40.0 c.c. water containing filtrable fever toxin and 40 organisms per cubic centimetre. Injection ratio 1 in 58. **B**, Rabbit, 2,448 gm. injected intravenously with 49.0 c.c. saline containing 950,000 organisms per cubic centimetre, but no filtrable fever toxin. Injection ratio 1 in 50. Both liquids injected immediately after heating. Interval between observations 30 minutes.

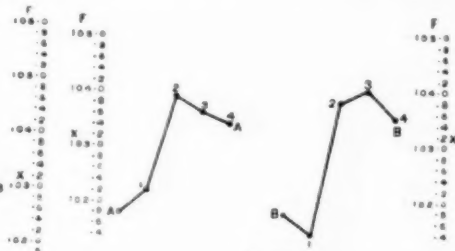


CHART 4.

Chart 4.—**A**, Rabbit, 2,278 gm. injected intravenously with 10.80 c.c. water containing 40 organisms per cubic centimetre and filtrable fever toxin. Injection ratio 1 in 211, before filtration. **B**, Rabbit, 2,335 gm. injected intravenously with 11.0 c.c. from the same water. Injection ratio 1 in 211, after filtration. Interval between observations 30 minutes.

sample of water with which the saline was made up had or had not been demonstrated. The theory, in fact, appeared to be based on the assumption that the presence of a large number of dead organisms is in itself sufficient to cause fever, whatever their source.

We therefore conducted control experiments to see if unbroken bacterial protein is necessarily pyrogenetic, and if the ordinary bacterial filter does actually render toxic solutions atoxic. We centrifuged 225 c.c.

of heated water, and 54 c.c. of heated saline, containing respectively 73,000 and 950,000 organisms per cubic centimetre, and injected the deposits. In neither case (Charts 1 and 2) did fever result. We also injected 50 c.c. of a specimen of saline containing nearly 50 million organisms (Chart 3). This saline was autoclaved immediately before injection. Again no fever resulted. Finally, we injected samples of water and of saline, both grossly infected, before and after filtration through white Doulton candles, and found that their fever-producing properties were practically unimpaired by passage through the filter (Chart 4).

Clearly, therefore, the theory that salvarsan fever is necessarily due to the actual presence in the solutions of dead micro-organisms

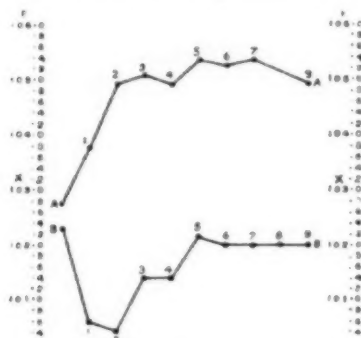


CHART 5.

Chart 5.—A, Rabbit, 2,324 grm. injected intravenously with c. 42.0 c.c. water containing filtrable fever toxin and 40 dead water-grown organisms per cubic centimetre. Injection ratio 1 in 50. B, Rabbit, 2,448 grm. injected intravenously with 49 c.c. pure saline containing no filtrable fever toxin but c. 1 million dead saline-grown organisms per cubic centimetres. Injection ratio 1 in 50. Interval between observations 30 minutes.

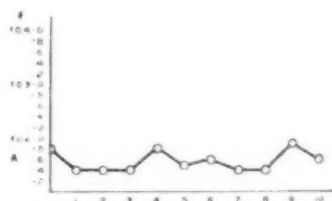


CHART 6.

Chart 6.—Distilled water, 1 in 5,180; 2,526 grm., A, 0.48 c.c. water.

capable of removal by hardware filters is not supported by our experiments. We do not, of course, assert that what we found to be true of organisms grown in water or saline in our laboratory is necessarily true of all organisms grown in water or saline. Injection of heated organisms that have been grown on nutrient media is known to give rise to fever, and from this fact no doubt arose the assumption that injection of organisms grown on water or saline and then heated must necessarily have the same effect. Since, then, this theory of salvarsan fever appears incomplete, explanation of its cause must be looked for elsewhere.

In December last [3] we showed that the pyrogenetic function of ordinary distilled water is often inversely proportional to the number of organisms present. Water, for example, containing forty dead organisms per cubic centimetre produced high fever, whilst an equivalent quantity of saline containing nearly a million dead organisms per cubic centimetre produced none (Chart 5). We also pointed out that an important factor in the production of fever after injection of sterilized water or saline is the presence of a heat-stable substance, of unknown source, incapable of removal by the centrifuge or the ordinary bacterial filter (Charts 6—11).¹ We now find that this pyrogenetic body is to a great extent, though not entirely, held up by Martin's gelatine filter. It is therefore a colloidal substance of small molecule. Since we could demonstrate its presence both in liquids grossly infected and in liquids practically bacteria-free, the problem is to explain how the

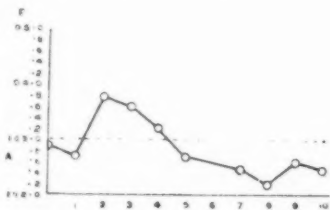


CHART 7.

Chart 7.—Distilled water 1 in 2,000; 2,250 grm., A, 1.10 c.c. water.

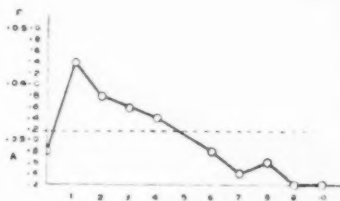


CHART 8.

Chart 8.—Distilled water 1 in 1,375; 2,363 grm., A, 1.71 c.c. water.

contamination arises. We find that if water be collected from the ordinary distilling apparatus found in laboratories and pharmacies and at once injected after sterilization, marked fever may follow, in spite of the fact that the water is sterile. This also applies to saline made from this water. We also find that water freshly distilled from a glass retort, and at once injected, does not contain this filter-passing pyrogen, and therefore does not cause fever, whether salt and salvarsan be added or not.

One possible suggestion, therefore, as to the explanation of salvarsan fever is as follows: The receiving tank in a good closed distilling apparatus is impervious to air infection except through the joint with the condenser, which being generally of cork should prevent entry of

¹ Charts 6—10 show the progressive amounts of fever produced by increasing quantities of toxic sterile water when injected in strict relation to body-weight, Chart 6 showing no fever owing to the small quantity injected.

organisms in the absence of reverse currents. When the apparatus is in use there is, of course, no reverse current. As soon, however, as distillation for the day is ended cooling takes place, and a reverse current, the action of which can be watched, is set up. Water in the receiving tank in consequence becomes infected from the air by aspiration. The next time the apparatus is used, unless the tank be meanwhile emptied, the freshly distilled water coming from the condenser is liable to contamination by passage through a residue that is readily shown to be pyrogenetic. Very few organisms can be found in the latter, because if the still is in daily use they are destroyed by the high temperature of the water coming from the worm when the condenser has become hot. The net result is that through repeated small increments of infection, when the apparatus is cooling, the water in the receiving tank becomes charged with this heat-stable toxin. This

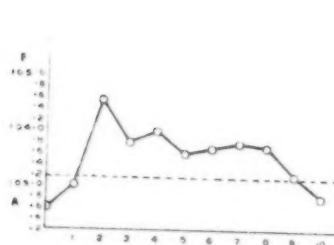


CHART 9.

Chart 9.—Effects of distilled water, 1 in 490; 2,450 grm.; A, 5.0 c.c. water injected.

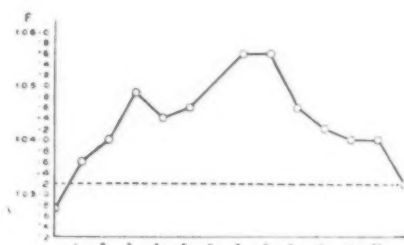


CHART 10.

Chart 10.—Distilled water, 1 in 58; weight of rabbit, 2,926 grm.; A, 50.40 c.c. water.

substance appears, in fact, to be a degradation product of air-borne organisms, themselves no longer to be found. Subsequent infection of this water in the laboratory, or of saline made from it, may of course occur if good conditions are not observed. Unless, therefore, control injections be made before the onset of secondary infection, a totally erroneous interpretation may be put on the fever that may follow injection of saline made with this water after secondary infection has occurred. If, on the other hand, water freshly distilled from glass, and proved to be free from this pyrogenetic substance by injection, be mixed with salt and exposed to laboratory air for several days, and injected immediately after autoclaving, fever may or may not result. If, however, a sample of this saline, if infected, be autoclaved, and after an interval of days be then injected, fever follows, apparently because in

the interval degradation products have now been extracted. The conclusion, therefore, appears to be that protein extractives derived from air-borne organisms are not present in sufficient quantity to cause fever if a sufficient time has not been allowed to elapse to permit of extraction. If, on the other hand, the organisms are killed, and if adequate time be allowed for extraction, degradation products make their appearance and fever will then follow injection (Chart 12).

Whether this explanation prove eventually to account for all the facts or not, it is certain that demonstration of the sterility of any given sample of water or saline affords no guarantee of the absence of this heat-stable pyrogenetic body. The presence or absence of this substance can be readily shown in an hour's time by the injection of rabbits, but

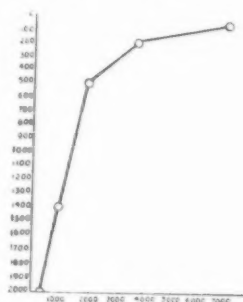


CHART 11.

Chart 11.—A rough curve illustrating the points shown in Charts 6—10.



CHART 12.

Chart 12.—**A**, Rabbit, 1,970 grm., injected intravenously with 78.0 c.c. of water. **B**, Rabbit, 2,083 grm., injected intravenously with 85.0 c.c. of water. **C**, Rabbit, 2,112 grm., injected intravenously with 87.0 c.c. of water. Injection ratios in all three, 1 in 25. Interval between observations 30 minutes. In **A** the water was taken direct from the receiving tank. In **B** the water was collected direct from the worm. In **C** the water was collected direct from a glass retort without the intervention of worm or receiving tank.

unless the volume of injection be graduated according to body-weight no reliable inference can be drawn, as our charts show.

It is, we believe, this substance, whatever its origin, that is largely responsible for salvarsan fever, salt fever, water fever, and many of the other types of injection fever referred to. This belief is based partly on the work we have outlined. It is also based on numerous experiments by which we find that it is very difficult to produce injection fever of any kind, apart from bacterial fever, if the water and saline used as

solvent or vehicle do not contain this pyrogenetic substance. These experiments, however, we are not at liberty to refer to further here as they have been submitted to another Society. The importance of recognizing its existence is, however, obvious. Although the explanation we have offered of its appearance in water and saline seems to be supported by the facts we have quoted, we cannot as yet be absolutely certain that this filter-passing toxin is of bacterial origin.

The method of preventing contamination of water or of saline by this fever toxin is fortunately simple. The use of freshly distilled water that has been collected from a receiving tank in connexion with the ordinary metal still is, as we have seen, not permissible, unless the tank is emptied and cleaned before use. If water be used immediately after distillation from a glass retort, fever does not follow the injection of salvarsan in saline made from it. If storage be desired, water distilled from glass should be at once collected direct into sterile vessels, which should then be immediately hermetically sealed and autoclaved. Samples of water prepared in this way on examination several weeks afterwards did not produce fever, either alone or in combination with salt. The use of sealed ampoules containing sea-water or saline has been practised in France for some years. In the case of saline, and often in the case of sea-water, each ampoule is labelled to the effect that it has been autoclaved. We recently examined some of these, and found that many of the ampoules contained saline and sea-water that were pyrogenetic. Either, therefore, the water when inserted already contained this pyrogenetic substance, or delay occurred between distillation and autoclaving. If delay does occur, or if the water be taken from an infected still, autoclaving is a distinct disadvantage, because the extraction of toxic degradation products appears to be then facilitated.

In discussing the causes of salvarsan fever it has often been suggested that a pyrogenetic substance may be set free from the spirochaetes destroyed, and that salvarsan fever may be, wholly or in part, a spirochaete fever. Before the latter view can be accepted it will be necessary to inject a suspension or extract of washed spirochaetes in pure saline or water. Until, however, this be done it is not possible to explain salvarsan fever by contamination of the water or saline alone, as Dr. McIntosh and his colleagues have pointed out. The evidence they have so far brought forward of spirochaete fever, though highly suggestive, is not convincing, because the two cases they quote were children. It is therefore possible that the fever observed in these two cases after injection of salvarsan was due to slight toxicity of the

solutions which was not detected by injection of adults. In other words, as we have shown, it is not safe to assume that any given saline is atoxic because it contains no organisms, and produces no fever when injected into a man weighing, say, 14 st. Injection of the same volume of the same saline into a child weighing, say, 6 st., may, if the water has been taken from the ordinary closed still, contain the pyrogenetic substance. Constant volume and inconstant weight are a fruitful source of error. On the question of spirochæte fever it is perhaps worth notice that Wechselmann met with no fever after injecting 150 cases with salvarsan in pure saline, a fact which throws some doubt on the ability of spirochætes to produce fever.

We conclude, therefore: (1) That there is at present no evidence that salvarsan fever is necessarily due to injection of organisms grown on water or saline; (2) that the presence in water or saline of a filter-passing pyrogenetic substance, which may or may not be a product of bacterial protein, is an important factor in the production of salvarsan fever and of many other types of injection fever.

In saying this, however, we wish to make it clear that our ability to demonstrate the fever-producing properties of this unsuspected contamination of watery solutions is the direct outcome of the observations made by Wechselmann and his supporters. Speaking for myself alone, if I had been aware of its existence when I advanced the autolytic theory of fever, I should not now be in the unenviable position of demonstrating to be false what I then believed to be true. To save other workers from a similar fate I am bound, therefore, to disclose the fallacies involved.

Note.—In speaking of fever throughout this paper we refer only to the presence or absence of fever occurring within one to six hours of injection.

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A Case of Diffuse Neurofibromatosis.

By J. M. BEATTIE and ARTHUR J. HALL.¹

THE patient, M. B., a female, aged 17, was admitted to Sheffield Royal Hospital on October 13, 1911, suffering from loss of vision and general weakness.

History given by the mother: She was quite well and like the other children until four years ago, when she had a "stroke." Her mouth was drawn to the right side, and her right eye bulged. The "stroke" came on whilst she was sitting down—she said her face felt funny, and at the same time she lost the use of the right arm and leg. Since then she has not been able to walk properly and has dragged her right leg in walking. For two years her sight has been failing: and her hands and arms have been getting very thin. One year ago a lump was noticed on one arm. Six months ago, lump noticed on the opposite arm. About the last week in September, 1911, she began to be very restless, with much twitching of the limbs, and grimacing. These movements became worse, and her manner quite childish. Three days later she suddenly became completely blind, and almost completely deaf. She has had severe pain in the head, both back and front; this has been worse at night. She is unable to stand up.

Personal history: She was not at all childish till the present illness. Menses have not occurred for three months.

Family history: Mother says, "All children have had lumps in the neck at birth; she herself had one; but all disappeared."

(N.B.—All these members of the family have been personally examined by one of us, and no trace of any tumours could be found.)

Condition on admission: She lies on her back with a vacant expression and is usually singing, or talking to herself, or shouting out for the nurse—repeating the same phrase over and over again at intervals. She is quite blind and very deaf, and is aware of this, for she says she can hardly hear her own voice. Her whole mental condition is curiously simple and childish, and she does not realize the gravity of her symptoms. She is very loving and strokes the nurse's hand or the doctor's, and says "Do make me better quick, doctor, I want to go to my sister's wedding." There is slight prominence of the eyes, slightly more on the right than

¹ From the Pathology Department, University of Sheffield.

the left. Vertical nystagmus. Marked choked disk both sides. Paresis of left external rectus. There is marked paralysis of the face on the left side—chiefly lower part, but cannot close the left eye. Deafness complete on left side, almost complete on right. No definite evidence of any involvement of other cranial nerves at this time. Trunk and limbs: There is no complete paralysis of any single limb, but general



FIG. 1.

Base of brain, showing tumours on cranial nerves.

muscular weakness is very great so that she cannot sit up. There is general wasting. Arms are extremely thin; wasting is particularly noticeable in both hands where there is extensive atrophy of the small muscles generally. There is marked inability to use the hands. Main en griffe. Reflexes not obtained. No sensory changes, no pains. Legs: General muscular wasting, particularly about the extremities; feet in position of talipes equino-varus and pes cavus marked on the left side.

Knee-jerks absent. Plantar reflexes are extensor, both sides. No sensory changes. No pains.

Distribution of tumours: Just above each elbow on the 'flexor surface' is a large oval firm swelling, movable under the skin. These are the largest that can be felt subcutaneously—up towards and in the axillæ many more can be felt, smaller in size. At each side of the neck similar smaller firm subcutaneous nodules can be felt. There is also one small one on the left side of the forehead. Over the right temple there is a roundish brown pigmented spot, not raised. On the right side of the neck there is a small nodule in the skin; when handled the girl said she had had that one since birth. This nodule was unfortunately overlooked at autopsy amongst the multiplicity of other tumours. It was distinctly in the skin itself or immediately beneath.

None of the tumours when handled caused any pain except that above the left elbow, which seemed to make her uncomfortable when moved.



FIG. 2.

Spinal cord (dorsal surface).

During her stay in hospital the symptoms steadily advanced. She soon became completely deaf, and had some difficulty in swallowing. There was also some loss of taste, as she complained that all food at all meals was "fish." On one day she developed Cheyne-Stokes respiration for a short time.

About November 6, 1911, she had some frontal headache for a day or two, and ceased to control the sphincters. Sensation to pain in the legs also seemed diminished and much delayed. The superficial plantar reflexes could not be obtained.

Death occurred on December 2, 1911.

At the autopsy extremely diffuse neurofibromatosis was found involving the cerebrospinal nerve-trunks almost universally. A detailed description of the sites of these very numerous tumours and thickenings is quite impossible. The tumours vary in size from an orange down to

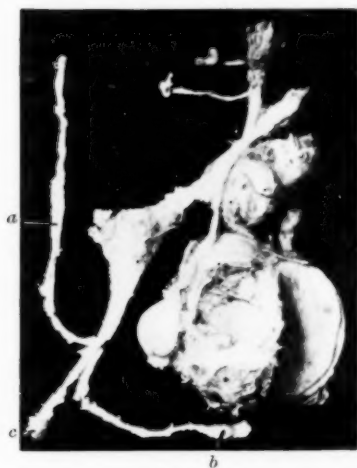


FIG. 3.

Large tumours on right lumbar plexus.
a and *b* should be parallel with *c*.



Left lumbar region.



Left arm

FIG. 4.

Tumours of nerves of left arm and left lumbar region.

a pin's head. They affect the nerves at their origin within the membranes, and at all points along their trunks. The largest are found on the more bulky peripheral nerve-trunks—viz., the nerves to the limbs, one lying on the right just inside the pelvis being considerably the largest—next a mass on the left anterior crural, and on the medians of the arms. Inside the cranium almost all the nerves seem to be involved, except the first and the sixth, but owing to the multiplicity of tumours and the displacement caused by them, it is not easy to say to which nerve each tumour belongs. The optic nerves have tumours on them in the orbits. Two large masses on each side seem to represent in front the fifth nerves, and behind the seventh and eighth—these latter being much the largest intracranial growths. In removing the brain it was necessary to cut parts of these away owing to their projecting into the canals by which the nerves leave the skull.

The amount of deformity in the pons and medulla caused by the growths is very considerable.

In the spinal canal the growths are most developed about the cervical and lumbar swellings—where they are so close to the cord that they appear to be actually parts of the cord, and are covered by the pia and vessels. At the right of the lumbar region there is a large rounded tumour just outside the dura.

The nerves of the cauda equina show large numbers of small swellings, giving them a beaded appearance, whilst lying rather behind these at the bottom of the cord is a single larger rounded tumour the size of a cherry.

Of the tumours on the peripheral nerves, the large one situated on the right lumbar plexus has undergone degenerative changes.

The fact that this condition is a generalized overgrowth of the nerve-sheaths rather than a simple tumour formation is shown everywhere by the thickening and deformity of the nerve-trunks, so that there are all gradations, from a nerve thickening to definite tumour formation. No tumours were found on the sympathetic system; none in any of the viscera.

Microscopically: Sections made from various nerves and tumours show uniformly the same overgrowth of fibrous tissue. The nerve-fibres are usually at one side of the tumour formation or they are separated by varying thicknesses of fibrous tissue. Sections from the median, stained by Weigert-Pal, show definite degenerative changes in some of the nerve-fibres. Nowhere is there any evidence of sarcomatous tissue. In the largest tumours of the right lumbar plexus simple necrotic degeneration has occurred.

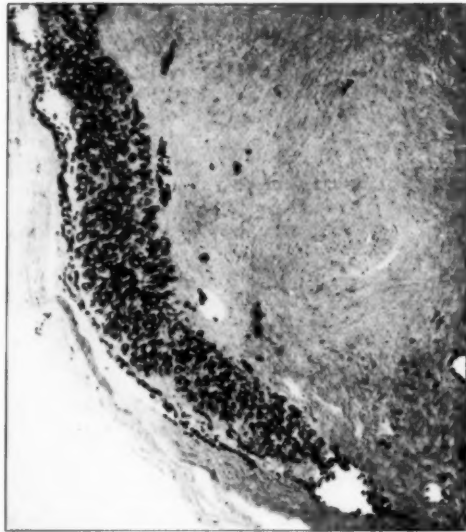


FIG. 5.

Section of nerve and tumour, showing the nerve pressed to one side, but not invaded by the tumour.



FIG. 6.

Section of a portion of the median nerve, showing definite degeneration (pale areas) in the nerve-bundles.

REMARKS.

Clinically, the most surprising feature was the almost complete absence of severe headache or vomiting. She is reported to have suffered from headache before admission, but during the time she was in hospital she hardly had any pain. Considering the comparatively rapid advance of symptoms of intracranial disease, the large mass of neoplasm under the tentorium, and the distortion which had been produced on the pons, medulla, and cerebellum, this seems difficult to explain.

Involvement of cranial nerves: Alexis Thomson, in his classic monograph on neuroma and neurofibromatosis, gives a table showing the relative frequency with which the cranial nerves have been found to be involved as follows:—

FROM FORTY-FIVE AUTOPSIES.

	Affected in		Affected in
X Vagus ...	29	II Optic ...	1
V Trigeminal ...	12	IX Glosso-pharyngeal ...	4
XII Hypoglossal ...	7	VIII Auditory ...	3
VII Facial ...	6	VI Abducens ...	3
XI Spinal accessory ...	6	IV Trochlear ...	1
III Oculomotor ...	6	I Olfactory ...	1

In our case the only cranial nerves which seem to have escaped are the olfactory and the sixth. As regards the question whether degenerative changes occur in the nerve-fibres or not, Thomson refers to several writers who deny that this occurs. We are satisfied that in our case there is evidence of degeneration having occurred, and this is supported by the typical wasting of the hand muscles observed during life.

As regards the important questions of when these changes began, and why they developed during the last few months with such rapidity as to prove fatal within a year of their being definitely recognized, we have no answers to offer. That the condition had existed for long without symptoms, and had developed with the onset of puberty, seems probable.

**Multiple Embolic Aneurysms of Pulmonary Arteries following
Thrombosis of Veins of Leg: Death from Rupture of
Aneurysm into Lung.**

By J. M. BEATTIE and ARTHUR J. HALL.

HISTORY OF THE CASE: H. W., a clerk, aged 21, was admitted to the Sheffield Royal Hospital under one of us (A. J. H.) on July 29, 1911. His medical attendant, Dr. W. C. Taylor, gave the following account of the case: On February 28, 1911, he began to have pain in the left leg so that he had difficulty in walking. This became worse, and a week later he had to take to bed and was found to have thrombosis of the veins of the left leg. On March 23, 1911, after his leg was, apparently, quite well, he had an attack of hæmoptysis with some shivering, and from that time onwards these attacks have recurred. About the beginning of May he went to Blackpool, where he was again laid up with attacks of shivering, hæmoptysis and pyrexia. The sputum was examined two or three times whilst he was there, but no tubercle bacilli were found. He stayed at Blackpool until early in July, and since then has been getting up daily, but still has the "shiverings," cough and hæmoptysis, together with pain in his left side. His fingers go cold, the nails go black and he shakes all over. These attacks occur quite regularly. He is not losing flesh and does not sweat.

Present condition (July 29, 1911): He is somewhat spare and pallid; there is no increased frequency of respiration; slight cough, worse at times; sputum chiefly mucus, with slight hæmoptysis almost daily. Chest: movements good and equal; no bulging or flattening: over the left first interchondral space there is slight pushing out of the surface during inspiration. Over a rounded area in the right first two interspaces in front, close to the sternum there is jerky, cogwheel breathing with prolonged and loud expiration, and in the lower part of the area occasional fine crepitations at the height of inspiration with an occasional rhonchus. Fine crepitations at the height of inspiration were also heard occasionally over the second left interchondral space. No other abnormal signs were observed on repeated examination. The abdomen and other parts of the body showed nothing abnormal. The temperature rose daily to 100° F., or 101° F., usually in the afternoon, coming to normal in the early morning. The heart sounds were normal.

The pulse varied from 90 to 110; soft and small. At irregular intervals he had a slight but definite rigor; this was always followed by an increase in the hæmoptysis. The sputum always negative. Cutaneous tuberculin reaction negative.

Progress of case: He was kept out of doors on the ward balcony, and his condition varied but slightly from week to week. Thus the week but one before his death he had a fairly severe rigor with a swinging temperature, whilst the week of his death the temperature

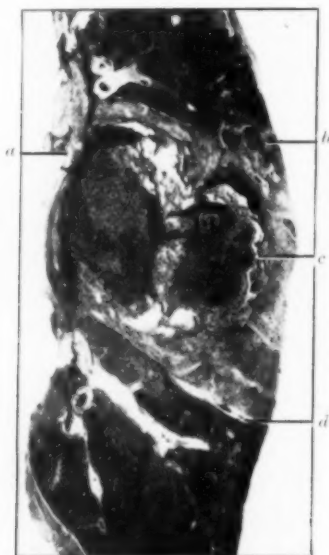


FIG. 1.

Large embolic aneurysm of right lung, which ruptured into bronchial tube — antero-posterior section. *a* = region of site of rupture, *b* = upper edge of compressed lung, *c* = aneurysm filled with organized thrombus in concentric lamellae, *d* = lower limit of compressed lung.

was much less, and he seemed better. On September 7, at 3.15 a.m., he was seized with profuse suffocative hæmoptysis, from which he died suddenly.

Autopsy: Both lungs are strongly adherent at the bases. On the surface of the upper lobe of the right lung is an area of a paler colour than the rest, occupying the inner half of the lower part of the front

surface, extending down to the sulcus separating the upper from the middle lobe. It measures about 5 cm. by 6 cm. superficially, is covered by rough and thickened pleura, and projects somewhat in its central part. On section (fig. 1) there is found lying beneath it a rounded mass of organized thrombus measuring about $4\frac{1}{2}$ cm. in diameter, sharply marked off from the lung tissue by a capsule. Its surface reaches at the nearest point to within about 0.5 cm. of the anterior surface of the lung, posteriorly it extends towards the root of the lung. The thrombus is concentrically laminated, dense and pale. In its centre there is an irregular cavity containing recent blood. The lung tissue immediately



FIG. 2.

Portion of right lung laid open, showing in outer parts organized thrombus in concentric lamellæ. At inner side irregular cavity containing recent blood.

around is compressed and pale and gives the appearance as of an old infarction. At the posterior mesial end of the thrombus the capsule appears to be excessively thin, and it is probable that it has here ruptured into a large division of a main bronchial tube and so led to the rapidly fatal hæmoptysis. It is a large healed aneurysm of the pulmonary arterial branch. In the right middle lobe, immediately below the above, there is a second similar but rather smaller aneurysm, also well filled with organized thrombus (fig. 2). In this case the sac of the aneurysm is well shown. The remains of the cavity, containing recent blood, are at the side of the thrombus, a sacculated aneurysm. The

MH—21a

lung tissue in the neighbourhood of this cavity shows some dark yellow pigment evidently the remains of old hæmorrhage into the lung tissue. The lung tissue around does not seem to be compressed. This aneurysm bulges into the right side of the pericardium, and the latter is adherent over the bulging. In various parts of the right lung there are thrombosed vessels—one large branch of the pulmonary artery being stuffed with organized pale thrombus—but there are no other aneurysms. The lung substance is extensively engorged with blood from the fatal hæmoptysis. In the left lung two or three smaller aneurysms can be seen. In one shown in the figure (fig. 3), a fusiform aneurysm with central

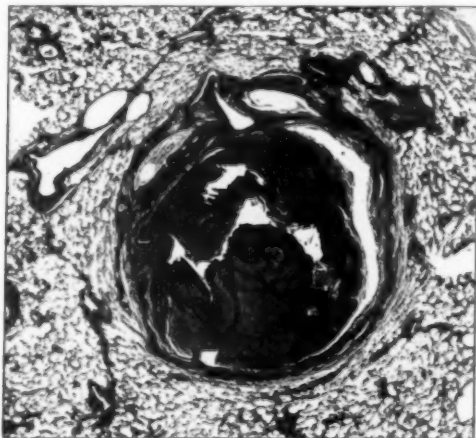


FIG. 3.

Small aneurysm of left lung. Central irregular cavity with organized thrombus around. The thrombus is retracted from the wall at one side.

cavity, the vessel opening into it could be distinctly traced and a probe passed along it. In the cavity of the right ventricle of the heart there is a warty organized thrombus, about the size of a pea, lying near the apex, otherwise the heart is normal. None of the valves are affected at all. No thrombosed vein was found in the leg. All the other organs appeared healthy. There was no infarction of the systemic arterial system. Unfortunately no bacteriological examination of the blood was made during life. Microscopical examination of the lesion in the right ventricle and of the aneurysms failed to show any evidence of micro-organisms.

REMARKS.

The starting point was a thrombosis of veins in the left leg, whether primarily due to the entry into the circulation of some micro-organism of low virulence from the skin or elsewhere, or whether secondarily infected, is uncertain. Four weeks later rigors and pyrexia showed that a general systemic infection had occurred, whilst hæmoptysis indicated local vascular lesions in the lungs. From that time onwards for five months these conditions remained practically unchanged—viz., a daily pyrexia with occasional rigors typical of a low form of septic infection, and frequently blood-stained sputa suggesting repeated pulmonary infarction. At the same time no trace of an endocardial murmur was found, though sought for carefully day by day.

He did not appear in any way worse the day before death than during the previous five months, and his death, from profuse hæmoptysis, was quite unexpected and not easy to explain until the autopsy.

It is obvious that this fatal suffocative hæmoptysis was pathologically distinct from the slight daily blood-stained sputa which had been going on more or less for five months. The latter was possibly of similar origin to that usually associated with infarction of the lungs, whilst the former was due to ulceration of the largest pulmonary aneurysm into a main branch of the right bronchial tube, and the process was pathologically identical with that seen in aortic aneurysms rupturing into a bronchus or elsewhere. The existence of embolic aneurysms was not diagnosed during life, nor was their true nature at first recognized when the lungs were removed from the body. They were thought to be sarcomatous growths.

Embolic aneurysms of the pulmonary arteries are extremely rare. Inquiries as to the existence of specimens made from the curators of twenty-one of the leading pathological museums of the United Kingdom, and a search through the literature of the subject, have enabled us to collect five more cases.

Case I (Thompson, *Medical Times and Gazette*, 1877, ii, p. 56).—Multiple aneurysms in the heart, lungs and cavity of cranium. History: Man, aged 20. Chest pain and dyspnoea, December, 1875; physical signs of acute endocarditis—hæmoptysis early; aphasia, April, 1876. Died June, 1878. Autopsy (Dr. S. Coupland) showed vegetations in right ventricle, which had ulcerated through the interventricular septum and infected the left heart also, leading to embolic aneurysms in the systemic vessels.

The specimen of the heart from this case is still in the Middlesex Hospital Museum, No. 983. Referring to the lungs the Report says

(right lung): "There were five saccular pouches—true aneurysms— . . . on different branches of the pulmonary artery, all possessing walls of immense thickness and all loosely attached to the tissues around. One was seated on the main artery supplying the middle lobe; it was of the size of a Barcelona nut, and lined by a layer of adherent fibrin, &c. In the left lung there was one aneurysm and several infarcts." In this case the infective agent had acted locally on the heart itself and brought the two sides of the circulation into direct connexion, so that multiple embolic aneurysms were found not only in the pulmonary arterial branches but also in the systemic.

Case II (Percy Kidd, *Transactions of the Pathological Society*, 1893, xliv, p. 47; specimen in Museum of Brompton Hospital, Catalogue No. 261).—Single woman, aged 22; dyspnœa and wasting twelve months; physical signs of endocarditis and pulmonary phthisis (tubercle bacillus +); vegetations in aortic valves extensive; patent ductus arteriosus, vegetations in pulmonary artery, near mouth of ductus. A single aneurysm, size of walnut, at apex of left lower lobe; filled with laminated thrombus; corresponding branch of pulmonary artery not obstructed. Infarcts in spleen, kidneys and small aortic aneurysm.

Case III (shown by Dr. Salusbury Trevor at Pathological Section, on February 20, 1912¹); the specimen is from St. George's Hospital Museum, No. 5631. Catalogue, Series VII, No. 65B).—"The specimen is the right lung, which is congested and œdematous. On the pulmonary artery within the lung are six aneurysms, the largest being the size of a tangerine, the others varying from that of a marble to a small pea. They are smooth-walled. In the largest was a small parietal projecting clot. They were found at autopsy in a married woman, aged 24, who had a history of six months' dyspnœa and weakness. Streptococci were found in the blood. The pulmonary valve was loaded with colossal vegetations of solid form, greenish-yellow in colour. The left lung contained three small aneurysms. Vegetations spread into the pulmonary artery from the valve. The wall of the large aneurysm, microscopically, is inflamed. Streptococci present in vegetations."

Case IV (under Dr. Laurence Humphry, Addenbrooke's Hospital; shown at Pathological Society of Great Britain and Ireland, at Liverpool meeting, January, 1912, by Dr. Malden).—For this abstract of notes we are indebted to Dr. Humphry. Clinical notes (short abstract): A lad, aged 18, admitted into Addenbrooke's Hospital, in July, 1909, suffering from Raynaud's disease of face and ears. No history of rheumatic fever. Præcordial pain, shivering and intermittent pyrexia

¹ *Proceedings*, pp. 155-8.

	Sex	Age	Symptoms	Physical signs	Duration	Cause of death	Lungs	Heart	Micro-organisms	Other morbid changes
(I) Thompson : <i>Med. Times and Gazette</i> , July, 1877	M.	20	Chest pains, dyspnoea, haemoptysis, aphasia	Heart murmurs, thrill, dull left base, Br., Br.	Six months	—	Right : five aneurysms of pulmonary artery, with walls of immense thickness; no thrombi. Left : 1 aneurysm, also plugs and infarcts Left : Single aneurysm, size of walnut at apex of left lower lobe, filled with laminated thrombus	Right ventricle : vegetations ulcerating through to left heart in two places	Not examined	Cerebral aneurysm; large infarct in spleen
(II) Kidd : <i>Transactions of the Pathological Society</i> , xlv	F.	22	Dyspnoea, wasting	Cardiac enlargement; multiple murmurs	Twelve months	—	Right : Six aneurysms, largest size of tangerine orange. Left : three small aneurysms	Left ventricle : Vegetations on aortic valves; patent ductus arteriosus; vegetations at mouth of patent ductus arteriosus Pulmonary valve loaded with vegetations extending into pulmonary artery	Not stated; tubercle bacilli in sputum	Small aneurysm of aorta; aortitis; infarcts spleen, kidneys; tubercular nodules in lungs
(III) Trevor : St. George's Hospital Museum, No. 5,631; shown at Pathological Society, Royal Society of Medicine, Feb., 1912	F.	24	Dyspnoea, weakness	?	Six months	—	Right : several small aneurysms, $\frac{1}{4}$ in. to $\frac{3}{4}$ in. diameter, larger branches and smaller affected. Left : none	Aperture of communication from conus of pulmonary artery to that of aorta, with fibrous tags on pulmonary side; patent foramen ovale	Not found in blood or after death in tissues examined	Old scars of healed tuberculosis in lungs; caseous bronchial gland
(IV) Humphry : Shown at Pathological Society of Medicine of Great Britain and Ireland, 1912	M.	18	Præcordial pain, shivering, intermittent fever, dyspnoea, attacks	Systolic thrill and whizzing murmur over pulmonary artery; later, soft systolic murmur over whole heart	Ten months	Sudden hæmoptysis	Right : three or four aneurysms, large, nearly filled with laminated thrombus. Left : two small aneurysms	Valves not affected; an organized warty thrombus in right ventricle	Blood not examined during life; no organisms found in heart nodule or aneurysms post mortem	None
(V) Beattie and Hall	M.	21	Thrombosis of leg veins, shivering, pyrexia, hæmoptysis	None in heart; slight patch of rough breathing in right chest	Six months	Sudden hæmoptysis	Right : three or four aneurysms, large, nearly filled with laminated thrombus. Left : two small aneurysms	Valves not affected; an organized warty thrombus in right ventricle	Blood not examined during life; no organisms found in heart nodule or aneurysms post mortem	None

were noted, and a marked systolic thrill and a rough whizzing systolic murmur over the pulmonary artery. Both the latter disappeared somewhat suddenly in the middle of August. Afterwards there was a soft systolic murmur of varying intensity over the whole cardiac area: he had attacks of severe dyspnoea from time to time. He recovered sufficiently to leave the hospital the following November, and was able to walk about but not to work. He was readmitted in April, 1910, for cough, with severe attacks of dyspnoea and pain in the chest. The heart condition had not changed. There were a few patches of diminished resonance with crepitation over both lungs. He died suddenly on May 6, in an attack of suffocative hæmoptysis. Several small aneurysms, right lung—none in left lung—measure $\frac{1}{2}$ in. to $\frac{3}{4}$ in. in diameter: contain irregular shreds of clot; aneurysm often seen at apex of infarct wedge; larger branches of main stem of pulmonary artery also affected. Heart: Patent foramen ovale; aperture in front of interventricular septum causing communication between conus of aorta and that of pulmonary artery; fibrous tags adherent round this on pulmonary side only.

Of these five cases it is to be noted that:—

- (1) All occurred in young adult life (18 to 24 years).
- (2) Duration from six months to one year from first onset of symptoms.
- (3) In two cases one lung only was affected—the left in Case II, the right in Case IV. In the other three cases the right lung contained larger and more numerous aneurysms than the left.
- (4) In two of the cases the aneurysms contained laminated thrombi—in the others there were occasional shreds of thrombus, otherwise they were empty.
- (5) In three cases the left heart was also affected. Case I: right ventricle primary, ulcerating through to left heart. Case II: left ventricle, aortic valves primarily affected; pulmonary artery secondarily involved through patent ductus arteriosus. Case III: from presence of embolic aneurysms in lungs only, and the very similar position of communicating aperture to that in Case I, and presence of tags only on pulmonary side, it suggests primary right ventricle ulcerating through to left. In the other two cases the infection areas are limited entirely to the systemic vein—right heart—pulmonary artery circulation.
- (6) In two cases an aneurysm ruptured into the lung, causing suffocative hæmoptysis.
- (7) Recurrent slight hæmoptysis, such as is seen in pulmonary infarction, is mentioned in two cases only.

(8) Streptococci were found in the living blood in one case only; in one case they were looked for but not found; in the other three no examination of the blood was made during life. Streptococci were found in vegetations in one case only. In two other cases they were looked for in the aneurysms and tissues but not found; in the rest they were not looked for.

In our case the most striking feature is the absence of vegetations on the pulmonary valves. Had the warty mass in the apex of the right ventricle been giving off portions of itself containing organisms sufficiently pathogenic to cause embolic aneurysms at their points of stoppage in the pulmonary stem, it seems very unlikely that these valves would have escaped entirely. Moreover, the warty growth in the right ventricle at the time of death was perfectly smooth, and had no rough shaggy surface suggestive of recent active processes.

It is more likely that the embolic aneurysms were originally started by a true embolus or emboli from the infective thrombus in the vein of the leg, and that these reached the right heart and pulmonary artery, at the beginning of the pyrexial period about a month after the beginning of his illness, when he began to get about, and probably dislodged the free end of the clot. This would explain the large size of the aneurysms and their being thoroughly filled with concentric layers of organized thrombus. It is possible further to explain his repeated hæmoptysis by emboli from the larger branch aneurysms being washed from time to time further into the pulmonary circulation, blocking terminal arteries and producing infarctions. If this is the correct explanation, the cardiac thrombus would then be not the intermediate stage between venous thrombosis and pulmonary aneurysms, but merely a portion of venous thrombus which had lodged in the laminae of the ventricular apex.

A Case of Multiple Mycotic Aneurysms of the Branches of the Pulmonary Artery within the Lung.

By R. S. TREVOR.

THE heart and lung shown were obtained from the body of a married woman, aged 24. She was admitted to St. George's Hospital on December 29, 1909, and died on January 15, 1910. She had had good health until two years before her admission when she had

"dysentery." At this time she was resident in Port Elizabeth, Cape Colony. Eight months before admission she had influenza, followed by right-sided pleurisy and hæmoptysis. She had not been well since, but was able to get about until three weeks before admission, when she was forced to lie up on account of swelling of the legs and abdomen. She had had one child fifteen months before admission.

On admission she was very anæmic and her skin was moist. Her teeth were bad, three being septic stumps. Lungs: Œdema of the

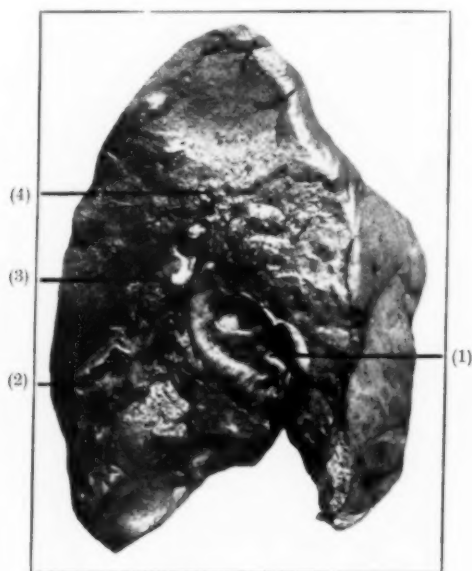


FIG. 1.

Photograph (much reduced) of cut section of the right lung. Four of the aneurysms are shown and numbered.

bases with moist sounds and dullness. Heart: Apex beat in fifth space in nipple line. Dullness one finger's breadth to right of sternum. First sound soft and followed at apex by a systolic murmur and loud second sound. Pulmonary second sound very loud. Diastolic murmur at the base to the left of the sternum in second and third spaces. Pulse rapid but regular, and markedly collapsing. Abdomen: No fluid; liver tender, not enlarged; spleen enlarged to below the umbilicus, hard and tender. Her temperature was irregular, and kept so throughout

the course of her illness. She had profuse sweats and an occasional rigor. On January 1, 1910, streptococci were found in her blood. She gradually went downhill and died two and a half weeks after admission.

Post-mortem Examination (forty-four hours after death).—Thorax : Adhesions present on both sides, especially on the postero-lateral aspect of the lungs and at the bases. There was about a pint of fluid in each chest. Lungs: The right weighed 28 oz. and the left 26 oz. Both were rather firm from chronic venous engorgement and were very œdematous. In both there were multiple aneurysms on the branches of the pulmonary artery. In the right lung shown (fig. 1) there are



FIG. 2.

Photograph of the heart, showing the massive vegetations on the pulmonary valves, and some of those in the pulmonary artery.

six aneurysms, the largest being in the lower lobe and, when fresh, of the size of a small tangerine orange. They are smooth-walled and were filled with soft clot chiefly of post-mortem origin. In places, however, there was a lining of ante-mortem yellow friable clot, similar in colour to the vegetations on the pulmonary valve. In the left lung there were three aneurysms, all of small size, the largest being of the size of a small marble. In the main branch of the left pulmonary artery was a large adherent vegetation of nodular shape, which formed part of a chain extending into the vessel from the vegetations on the pulmonary

valve. The pericardium contained an excess of fluid. The heart shown (fig. 2) weighed 15 oz. There was a marked prominence and bulging of the conus of right ventricle, which was in contact with the chest wall. Both ventricles, but especially the right one, are dilated and hypertrophied. Slight fatty change was visible when the heart was first opened. The pulmonary valve is disorganized by huge vegetations which are firm and greenish-yellow in colour. Further vegetations spread into the main trunk of the pulmonary artery, and they formed a complete chain into the left main branch. On the aortic valve two similar, but smaller, vegetations are present. The other valves are free. The aorta was thin and smooth, with traces only of early atheroma. It was free from aneurysms. No other aneurysms were found in the body. The abdominal organs were cardiac and the spleen, in addition, was much enlarged but free from infarcts. No septic focus was present in the body other than the dental caries. The head was not examined.

On microscopical examination streptococci were found in the vegetations on the pulmonary valve, but not in the wall of the aneurysms examined.

I am indebted to Dr. Hunt, of St. George's Hospital, for the following report on the streptococcus obtained from the blood: "As the result of the venipuncture on December 30 a streptococcus, Gram-positive, was obtained in cultures. In autoclaved litmus-broth-sugar tubes it gave an acid reaction with lævulose, lactose, raffinose, maltose, glucose, saccharose, and galactose; and no acid reaction with inulin, salicin, and mannite. It differed from the *Streptococcus pyogenes* of Gordon, Andrewes, and Horder by fermenting raffinose; from the *Streptococcus faecalis* (Andrewes) by not fermenting salicin or mannite; and from a pneumococcus by not fermenting inulin."

I have only been able to find the record of one other case of mycotic aneurysm of the pulmonary artery as having been shown to the Pathological Society—viz., the case recorded by Dr. Percy Kidd.¹ This case is remarkable in that the infective vegetations were on the aortic valve, not on the pulmonary valve. Vegetations were present in the aorta as well as round the orifice of a patent ductus arteriosus, through which the infective embolus must have reached the pulmonary artery. There was also a small sacculated aneurysm of the aorta just above the opening of the patent ductus.

My thanks are due to Dr. Ogle for permission to show the specimens.

¹ Kidd, *Trans. Path. Soc., Lond.*, 1893, xliv, p. 47.

Pathological Section.

March 19, 1912.

Dr. R. T. HEWLETT, President of the Section, in the Chair.

The Incidence of Streptococci in Urine.

By H. WARREN CROWE.

It is my desire to present a short survey of investigations in progress, rather than a full and considered report on a completed piece of research.

My interest in the bacteriology of the urine arose in the first place from the accidental discovery that the growth of organisms of the streptococcal group is prolific on egg medium. I have since found that Dr. Fleming uses Dorset's recipe for the culture of streptococci.¹ He adds a small amount of neutral red, by means of which streptococci are easily isolated, for their colonies appear red, and are surrounded by a vivid crimson area. I have adopted his method for isolating these organisms.

It was particularly the urine to which my attention was directed, since it was in an attempt to isolate tubercle bacilli from a case of tuberculous kidney that streptococci were first found to grow in such a prolific manner. In this particular case (Table I (A), 1) an autogenous streptococcus vaccine was given with happy results.

The next case (Table I (B), 16) in which I investigated the urine, and this most fortunately, was that of a woman who suffered from chronic tonsillar pain, rheumatism, lassitude, and headache, and who had been treated, without much benefit, by paradontal streptococcus vaccine, and

¹ Goadby speaks of the use of the egg agar for the culture of streptobacillary organisms [4].

also an autogenous vaccine prepared from a streptococcus isolated from the tonsillar crypts. An organism, similar to the one which occurred in the former patient, was found, and a vaccine was used with extreme success. I was particularly struck by the difference in the effect of this vaccine and the two former.

Further cases were then investigated, and Table I deals with twenty-one women and thirteen men, picked cases, whose symptoms suggested the possibility of bacterial infection. From the urines of eighteen of the women and eight of the men streptococci were isolated. Twenty-two patients were treated by vaccines, mostly autogenous. Four had tuberculous kidneys, two cystitis (vaccines of *Bacillus coli* were also given to these), and two suffered from nervous diseases, but a large proportion (twelve in number) presented a collection of symptoms which were indefinite enough when regarded separately, but in conjunction led me to examine the urine for bacteria. The majority complained of rheumatism, either slight or severe. There occurred frequently unpleasant cardiac sensations, varying from slight palpitation to pseudo-anginal attacks. A history of headache, or a sense of fullness or heat in the head, indigestion, and frequency of micturition could usually be elicited, and in a few an irritable roughness of the skin, with slight erythema, was noted, but common to all was a general lassitude. The last was mostly the cause of their seeking advice. Under vaccine treatment the symptoms subsided in a most gratifying manner, and a general feeling of well-being supervened.

To find as many as twenty-six urines infected by the same organism or similar organisms out of a total of thirty-four, and these organisms unmistakably pathogenic, led to the investigation which is the subject of this paper. At the outset a difficulty was met with. The old cultures, which had been kept going, were examined, but they were all found to be contaminated by diphtheroids, from which it was impossible to separate them. These diphtheroids had been noted occasionally during vaccine work, and were thought to be involution forms of the streptococci. They seemed to conform to the two varieties described by Pfeiffer [8] as occurring in 87 per cent. of male urethræ; also probably to those noted in Priestley's list given before this Society recently and indicated by the number G8 and G6 [9]. Since the cultures were lost, memory and a few notes must supply the information in regard to these vaccine cases. One feels greatly to blame in not having secured a careful record, but unfortunately the scientific value of vaccine work is impaired by the fact that a recognition of the organism is unnecessary.

I can therefore only make the following remarks with any degree of confidence :—

(1) One organism belonging to the streptococci varying in form and growth, or several different organisms, were cultured. Vaccines were prepared and administered to people chiefly afflicted with rheumatic symptoms, and the treatment met with success.

(2) In a few cases regular opsonic curves varying in a rational manner with the symptoms and with the inoculations were obtained.

(3) The effects, immediate and remote, of the vaccine left very little doubt as to the pathogenicity of the organism or organisms and their connexion with the symptoms.

Several urines of patients who had been treated were now examined, but only one was found to yield a growth of streptococci, and since no further cases presented themselves for treatment, the next step undertaken was to determine the incidence of streptococci in the urine of normal and hospital patients.

A series of urines from nine men and twenty-five women were obtained through the kindness of the Medical Officer, Dr. Sandford, from the Devonport Infirmary. Among the men four were sterile; five contained strepto- or diplococci. Among the women two were sterile, nineteen contained streptococcal or streptobacillary forms. I was not satisfied that these were uncontaminated with urethral or vaginal organisms, as the percentage was so great, and many other forms occurred which were unknown to me, so that it was determined to proceed further, and to take great care in order to avoid contamination. The only case I would draw attention to was one where a diagnosis of acute rheumatism was given, and in this case no streptococci were found. This struck my attention, since patient 11, Table I (A), had had acute arthritis simulating gout, and his urine was also sterile. His attacks were cut short on several occasions by doses of paradontal streptococcus vaccine. Later, during convalescence, I recultured his urine, and then found streptococci present. He is now having a stock streptococcus vaccine made from the germs isolated from urines.

The next series were from ten women, hospital cases. They also proved disappointing, as Gram-negative bacilli appeared in all except one, suggesting faulty catheterization. In one only a streptococcal organism was found.

From this time onwards observations were confined to males. By the courtesy of the Naval Authorities I was enabled to obtain two series of urines from the Royal Naval Hospital in Plymouth. The first

were taken from fifteen hospital patients; of the second series thirty-seven were normals from the sick berth staff, and fifty-three were from patients. All were examined by culture on egg medium. Instructions were given that the latter portions of the urine were to be passed direct into a sterile bottle.

Series I.—In one case only was a streptococcus isolated, but in seven of the cases an organism grew which corresponds remarkably with the *Streptobacillus urethræ* of Pfeiffer [8]. This had been already described (according to Pfeiffer) by Lustgarten and Mannaberg [7] and also by Faltin [3] as a streptococcus. Leaving the question open, I will refer to it by Pfeiffer's name to distinguish it from the organisms isolated from uncontaminated urine. It is, however, a useful organism to recognize in judging of the reliability of a series, as Pfeiffer found it in 42 per cent. of normal male urethræ. By the frequency of this organism, doubt was thrown on the urines in this series. On making inquiries I found that the order had been given that when a certain amount of urine had been passed the urethra should be compressed and then some of the remainder passed into a sterile bottle. Doubtless all possible hiding places in the urethra were thoroughly flushed out by the sudden distension, and in fact, many and wonderful were the growths obtained.

Series II.—The mistake in Series I was avoided, and I feel the more able to rely on these urines, as neither the *Streptobacillus urethræ* nor the diphtheroids appeared in any of the normals. Four distinctly different organisms could now be distinguished: (1) a diplococcus growing in short chains; (2) a staphyloid coccus; (3) the *Streptobacillus urethræ*; (4) a typical streptococcus, consisting of biscuit-shaped cocci, ten to twenty in a chain. The first mentioned was undoubtedly the one usually associated with chronic rheumatism, the last mentioned is very rare in urine. In about 200 I have seen it twice, but in one of those cases a vaccine was used with distinct effect. In regard to the second, I must leave the question very much undecided, as it might easily be held to be a staphylococcus, yet in sugar broth chains are seen, and it is a noteworthy fact that in two vaccine cases two million caused most unpleasant reactions. The following descriptions must be taken as tentative, since many strains have not as yet been examined.

The diploid form of streptococcus occurs as lanceolate diplococci in short chains in the urine, resembling pneumococci, their appearance often suggesting a capsule. They vary in size, but average $1\ \mu$ by $2\ \mu$ long. This organism is seldom actually found, except on cultivation, as the number of germs usually

is extremely limited. Growth on agar is scanty or absent, but after cultivation on egg, and transference to agar for twenty-four hours, the slope will be found to be covered with extremely minute, convex, glistening translucent colonies, of the appearance of streptococci in general. Later subcultures on agar appear either as very fine pin-point colonies or as large ground-glass masses. The former show, microscopically, the same characteristics as the organism in urine, though without any suggestion of a capsule. The chief points to notice are the parallel position of the cocci, which lie side by side in a chain, instead of end to end. The latter, microscopically, resemble the next organism to be described, and unless care is taken confusion may arise between the two. The colonies on egg (described below) should prevent any mistake. Gelatine growths appear as minute specks in about three days. There is no liquefaction. Sugar broth shows chains, and in blood broth pairs of lanceolate diplococci, closely resembling the pneumococci, are the feature. Blood is hæmolyzed.

The *staphyloid coccus* occurs as a perfectly round coccus in short chains or pairs, Gram-positive, but when subcultured tends to decolorize and take on the contrast tint. It is non-capsulated. When growing on artificial media it varies greatly in size from 0.5μ to 2 or 3μ . The growth on agar after egg culture is much more rapid and far denser than any of the other organisms here described. Twenty-four hours growth on agar reveals convex, translucent, glistening colonies. On gelatine slopes this organism, unlike the streptococcus, shows visible growth after twenty-four hours. Minute convex colonies, smooth edges and glistening surfaces. No liquefaction. In gelatine stab cultures, after twenty-four hours, very minute creamy points may be seen the whole length of the stab. Growth on nasagar is free, the colonies having a milky opacity. The colour of this and the former, when treated by the differential strain mentioned in text, is entirely red. On neutral red egg growth is remarkable, and the characteristic colonies obtain dimensions of 0.5 mm. after twenty-four hours. Under the microscope a great variety of forms are seen, some large and round, a few oval. Involution forms are numerous. Grows at room temperature best at blood heat. Blood is hæmolyzed where the colonies are dense, but no hæmolysis occurs around scattered colonies.

The *Streptobacillus urethræ* occurs in long chains, which are often coiled into tangled masses. The individual organisms are twice as long as they are broad, and ovoid with somewhat pointed ends, breadth about 1μ . They are Gram-positive. When stained with methylene blue they show polar staining; under the differential stain (described below), entirely blue. On agar the colonies are minute, convex, glistening, translucent growths, much smaller than those of the staphyloid coccus, smaller even than the diploid. On neutral red egg medium the colonies have raised central points, and broad, flat, thin edges, which after forty-eight hours sink in, except at the extreme edge, which appears thickened and raised. The neutral red is strongly reduced. Blood is hæmolyzed. This organism, under the microscope, appears

smaller and much more coccoid when growing on artificial media, and the chains are not so long or so thickened. It also tends to lose the violet when stained by Gram. Growth in blood broth, small lanceolate diplococci, resembling pneumococci, appear grouped in short chains or masses. (Pfeiffer describes long chains; these I have not seen.) On no artificial medium does this organism retain the characteristic appearance it has when seen in the urine. It most decidedly has a capsule. On the whole I believe it to be Pfeiffer's streptobacillus.

The fourth organism, which I distinguish as the *Streptococcus ? salivarius*, is found in the urine in chains of varying size. Individuals are most frequently lemon-shaped, but diplococci and large forms occur, some three or four times as long as they are broad. The usual size is about $1.9\ \mu$ by $1.5\ \mu$. When stained each pair often appears as a single coccus. On egg medium or nasagar the first culture shows longish chains of irregular cocci, and many involuting Gram-negative forms. When transferred to agar growth resembles that of other streptococci. Gelatine cultures develop slowly. Smears from agar show numerous masses of chains of cocci, varying in their Gram-staining. In later subcultures the cocci become more irregular and much smaller, in contradistinction to the other organisms described. On neutral red egg the colonies appear at first as small dots, growing slowly. They increase after two or three days to a large size, and are roughened, giving the appearance of ground glass. They are the thinnest and the flattest of these colonies, and are extremely characteristic. In shape the colony closely resembles that of a urethral diphtheroid (G 8 in Priestley's list [9]), but the latter is smooth, and glistening on the surface. Neutral red is not reduced in the earlier cultures. Later cultures, however, frequently turn the medium crimson.

For practical purposes the following points are the most important:—

(1) The first two usually occur in such small numbers that, as a rule, they are not seen in smears of urinary deposit. After culture on egg, colonies are easily picked out. If these are transferred to agar, growth is hastened, and after twenty-four hours sufficient is obtained for vaccine preparation.

(2) *Colonies on Neutral Red Egg Medium*:—

Diploid Streptococcus.—A raised, crimson, papillated colony, resembling a flattened cottage loaf. Crimson areola.

Staphyloid Coccus.—A very flat colony with a large rose-red, glistening papilla in the centre. It might be likened to the shovel hat of a priest. In subcultures the brim of the hat disappears, and a round, raised, rose-red colony remains. There is no reduction of neutral red in the vicinity. The egg is indented.

The *Streptobacillus urethræ* shows a crimson colony with a small central papilla, and on the outside a raised ring. Crimson areola marked.

The fourth streptococcus gives an extremely flat colony, which does not take up neutral red, and has no papilla, but the whole surface is finely corrugated. No crimson areola in first cultures. This appears in subcultures.

Slides of the diploid streptococcus show egg-shaped cocci in groups and short chains. The individuals mostly lie with their longest diameter at right angles to the chain, giving an appearance of ovoid "bodies" laid side by side. Strongly Gram-positive, entirely red by the following differential stain: hot Loeffler's methylene blue, followed by cold neutral red and differentiated with spirit.

The staphyloid organism is usually round. Size varies greatly. Involution forms common. It is stained by Gram's stain, but it is strongly tinged with contrast stain; entirely red by the differential stain.

The *Streptobacillus urethræ* shows many bacillary forms and is very minute. Gram-positive, some individuals completely decolorized. Remains blue with the differential stain.

The fourth is much larger, occurs in long chains of ovoid members, many involution forms, and Gram-negative individuals interspersed in the Gram-positive chain. On further culture each coccus becomes biscuit-shaped, and then by the differential stain shows red with a blue centre.

Of the thirty-eight normal men from the Naval Hospital, twenty-three were sterile, the diploid streptococcus occurred in three, the staphyloid coccus in four.

Of the fifty-three patients sixteen were sterile, eleven gave the diploid streptococcus, and ten gave the coccoid organism. In five the *Streptobacillus urethræ* was found, and in one the fourth streptococcus.

If reference is made to Table II, in which patients have been grouped according to their diseases, it is of interest to note that the majority of these organisms were found in slight ailments, gastric diseases, epilepsy and morbus cordis, and that the smallest percentage of all occurred amongst those suffering from acute rheumatism and from nephritis.

The last investigation carried out was on twenty-two healthy normal men. All were asked if they were troubled with rheumatism—five admitted that they were, though otherwise quite well. In one case only were streptococci found, the diploid variety. This man was a rheumatic. The whole of the remainder were sterile.

The characteristics of these organisms are displayed in Table III (A) and (B). I must, however, expressly state that the sugars were

from English firms, and if Dr. Gordon [5] is correct, the reactions must be taken with reserve. In other respects his method [6] has been followed.

Investigations into these organisms are still in progress, and in fact the bacteriology of the urine opens up such a wide field that one hesitates to make any pronouncement as to their identity, but one cannot help being struck by certain resemblances.

The diploid streptococcus follows the *Streptococcus faecalis* (as described by Dr. Andrewes [1] and Dr. Gordon [5 and 6], and also may be identical with the diplococcus described by Dr. Dudgeon [2], though this latter seems more likely to be the *Streptobacillus urethrae* under conditions of heightened virulence.

The staphyloid organism shows the reactions of the *Streptococcus pyogenes*, but also, be it noted, of certain staphylococci.

The fourth organism is possibly the *Streptococcus salivarius*.

These points are brought out in the latter part of Table III.

To summarize :—

(1) Two distinct cocci occur in the urine with comparative frequency, and both are probably streptococci.

(2) When certain symptoms suggesting slight toxæmia are associated with chronic rheumatism, streptococci may usually be found in the urine. Vaccine treatment in such cases is remarkably beneficial.

(3) In acute rheumatism the organisms described are usually absent from the urine.

(4) The isolation of the organisms and the preparation of vaccines are greatly facilitated by the use of neutral red egg medium.

(5) In general, if one is justified in drawing any conclusions from such a small number of cases, streptococci are met with in the urine more frequently in slight ailments than in severe diseases.

It is my hope that I have made out a case for systematic cultural examination of urine, whether attention is directed thither by symptoms or not, with the likelihood of its proving a fruitful field, both from the pathological and the therapeutic standpoint.

In conclusion, I must express my gratitude to all those through whose kindness I have been able to obtain material, to Dr. G. F. Leicester for his invaluable assistance in working out the organisms, and also to Dr. Iles and Dr. Brunwin in the laborious task of culturing each specimen of urine.

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TABLE I.—(A) MALES.

No.	Symptoms	Streptococci in urine	Coliform organisms in urine	Urine sterile	Treated by vaccines of urine organisms	Result and remarks
1	Tuberculous kidney and phthisis	+	-	-	+	Both lungs and kidney improved
2	Subacute mania	+	-	-	+	Indefinite; urine sterile
3	Gunshot wound, fractured pelvis; pus in urine	+	+	-	+	Streptococcus not isolated; improved under <i>Bacillus coli</i> vaccine
4	This case—emphysema—had streptococci in the sputum	-	-	+	-	These cases were examined for streptococci in urine, as the organism was pathogenic elsewhere
5	Pyorrhæa; streptococci	-	-	+	-	
6	Suppurating parotitis (for years); streptococci	-	-	+	-	
7	Bronchitis, aged 6; streptococcal infection	-	-	+	-	
8	Tonsillitis (acute); not examined	-	-	+	-	Treatment refused
9	Lumbago and sciatica, gastritis	+	-	-	-	
10	Muscular pains, headache, gastric catarrh	+	-	-	+	Treated and improved by paradontal and urinary stock vaccine
11	Acute "gout"; no organisms at first, though a blood culture taken and urine examined	+	-	-	+	During convalescence streptococci appeared in the urine; treatment markedly successful with paradontal vaccine and later streptococci from urine
12	Lumbago, lassitude, dyspepsia, cardiac neuroses	+	-	-	+	Under treatment; improving
13	Very acute muscular rheumatism, no fever, stiffness of joints, dyspepsia, cardiac neurosis	+	-	-	-	Intends undergoing treatment in the next attack

TABLE I.—(B) FEMALES.

No.	Symptoms	Streptococci in urine	Coliform organisms in urine	Urine sterile	Treated by vaccine of urine organisms	Result and remarks
1	Tuberculous kidney; tubercle bacilli in urine	+	—	—	+	Definite reaction follows vaccine
2	Tuberculous kidney (old); new lassitude	+	—	—	+	Inconclusive
3	<i>Tuberculous kidney, rheumatism, headache, lassitude, frequency of micturition</i>	+	+	—	+	Very good, rheumatism disappeared, kidney pain and lassitude abolished
4	<i>Cystitis, skin rough, cardiac sensations, rheumatism, frequency of micturition, lassitude, headache</i>	+	+	—	+	Excellent and symptoms disappeared
5	Very acute cystitis with rigors	+	+	—	—	Streptococci seen but not isolated
6	<i>Slight petit mal, cardiac neurosis, headache, rough skin, indigestion, extreme lassitude</i>	+	+	—	+	Improved, treatment refused after a short time
7	Tonsillitis, pyrexia, girl, aged 7	+	—	—	+	Excellent
8	Hæmaturia; ? sarcoma of bladder	?	+	—	—	Not treated, urine full of a variety of organisms
9	Acute sciatica, insomnia	+	—	—	+	Improved slightly
10	Colitis, cholecystitis, abdominal pain	+	+	—	+	Much improved by vaccines of <i>Bacillus coli</i> and streptococcus
11	General severe eczema	+	—	—	+	Skin lesions, staphylococci and streptococci; urine, streptococci only; under treatment
12	Arthritis following parturition, four years previously	+	—	—	+	Under treatment; unusual form of streptococcus
13	Pernicious anaemia; ? tubercle bacilli in urine	+	—	—	—	Soamin rendered urine sterile
14	Dyspepsia, cardiac discomfort	—	—	+	—	These were the only symptoms
15	<i>Rheumatism, cardiac sensations, frequency of micturition, dyspepsia, lassitude, headache, dysmenorrhœa</i>	+	+	—	+	Excellent, after a large dose of coli vaccine, agglutinated dead <i>Bacillus coli</i> found in urine
16	<i>Rheumatism, tonsillar pain, cardiac neurosis, rough skin, frequency of micturition, "heat in temples," dyspepsia, lassitude</i>	+	—	—	+	Most satisfactory; all symptoms disappeared
17	<i>As 16, but no roughness of skin or dyspepsia</i>	+	—	—	+	Declares herself quite cured
18	<i>Said to be "Graves's" disease, she has all the symptoms of 16 and 17 and pseudo-anginal attacks</i>	+	—	—	+	Under treatment; rapidly improving, after a dose feels headache worse
19	<i>Recurrent nasal catarrh and all symptoms of 16 and 17, but skin quite normal</i>	+	—	—	+	<i>Bacillus septus</i> and streptococcus vaccine, very much improved
20	<i>Another case of the same symptoms</i>	+	—	—	+	Stock vaccine; cured
21	Dilated heart, rapid pulse, fine tremor	—	—	+	—	Catheter specimen

Those cases showing the collection of symptoms mentioned in the text are in italics.
The total of these in the whole table is 12.

TABLE II.

Disease	Sterile	Strepto- coccus, diploid form	The staphyloid coccus	Strepto- bacillus urethrae	Strepto- coccus ? mili- varius	Coliform
<i>Digestive system—</i>						
Jaundice	+	+	+	+	+	+
Gastric ulcer	+	+	+	+	+	+
Gastritis	+	+	+	+	+	+
<i>Slight ailments—</i>						
Catarrh	+	+	+	+	+	+
Hysteria	+	+	+	+	+	+
Catarrh	+	+	+	+	+	+
"	+	+	+	+	+	+
Sore throat	+	+	+	+	+	+
Catarrh	+	+	+	+	+	+
"	+	+	+	+	+	+
"	+	+	+	+	+	+
"	+	+	+	+	+	+
Tonsillitis	+	+	+	+	+	+
Catarrh	+	+	+	+	+	+
"	+	+	+	+	+	+
Eczema	+	+	+	+	+	+
Vaccinia	+	+	+	+	+	+
<i>Chest diseases—</i>						
Influenza	+	+	+	+	+	+
Bronchitis	+	+	+	+	+	+
"	+	+	+	+	+	+
Pleurisy	+	+	+	+	+	+
Pneumonia	+	+	+	+	+	+
Influenza	+	+	+	+	+	+
Pleurisy	+	+	+	+	+	+
? Tubercle	+	+	+	+	+	+
Bronchitis	+	+	+	+	+	+
Pneumonia	+	+	+	+	+	+
Influenza	+	+	+	+	+	+
Bronchitis	+	+	+	+	+	+
Pneumonia	+	+	+	+	+	+
"	+	+	+	+	+	+
<i>Morbus cordis—</i>						
M.C.O.	+	+	+	+	+	+
"	+	+	+	+	+	+
M.C.F.	+	+	+	+	+	+
M.C.O.	+	+	+	+	+	+
"	+	+	+	+	+	+
"	+	+	+	+	+	+
"	+	+	+	+	+	+
<i>Acute rheumatic conditions—</i>						
Acute rheumatism	+	+	+	+	+	+
"	+	+	+	+	+	+
"	+	+	+	+	+	+
Gonorrhoeal rheumatism	+	+	+	+	+	+
Acute rheumatism	+	+	+	+	+	+
<i>Diseases of kidney—</i>						
Nephritis	+	+	+	+	+	+
"	+	+	+	+	+	+
Albuminuria	+	+	+	+	+	+
Nephritis	+	+	+	+	+	+
<i>C.N.S.—</i>						
C.N.S. ?	+	+	+	+	+	+
Epilepsy	+	+	+	+	+	+
"	+	+	+	+	+	+
<i>No diagnosis—</i>						
No diagnosis	+	+	+	+	+	+
"	+	+	+	+	+	+
"	+	+	+	+	+	+
Total	16	12*	11*	5	1	9

* One doubtful.

TABLE IIIA.—MORPHOLOGY.





No.		Streptococcus, diploid form, (the organism usually associated with the symptoms described in the text)	The staphyloid coccus	<i>Streptococcus urethrae</i>	<i>Streptococcus soliviridis</i>
1	Morphology in urine	...	Short chains of round cocci	Long chains	Large, lemon-shaped cocci in chains; involution forms
2	Morphology of cultures on agar	(a) Fine colonies, diplo-cocci; (b) large colonies like staphyloid coccus Several days	Great variation in size, short chains	Minute diplococci, bacillary forms, parallel arrangement	Biscuit-shaped, smaller cocci in medium chains
3	Morphology of cultures on gelatin (not liquefied by any)	Uniformly turbid, short chains	Good growth in twenty-four hours in chains	Very slow	Very slow
4	Morphology of cultures on sugar broth	Uniformly turbid, short chains	Uniformly turbid, some in chains	Uniformly turbid, short chains	Uniformly turbid, chains
5	Morphology of cultures on blood glucose broth	Large lanceolate diplo-cocci in short chains	Round cocci, some in chains	Minute diplococci, short chains	Large, biscuit-shaped diplococci in medium chains
6	Morphology of cultures on egg medium	Circular, papillated, raised colonies	Raised, glistening colonies, with a flat edge, this is lost later; egg indented	Circular colony like a draughtsman, raised centre, raised edge	Irregular shape, very flat corrugated surface
Diagnostic		(a) Shape (imaginary section) 			
7	(b) Colour of colony	Crimson	Rose-red	Crimson	Yellow, then crimson
8	(c) Reduction of neutral red	+	-	+	- then +
9	Lanceolate and bacillary forms	+	-	+	- in culture, + in urine
9	Capsulated ...	-	-	-	-
9	Staining reactions to—	Not tinged by contrast colour	Tinged by contrast colour	Gram-negative forms appear	Gram-negative forms appear
9	(a) Gram (all positive)	No polar staining	No polar staining	Polar staining	No polar staining
9	(b) Loeffler's methylene blue	All red	All red	All blue	Red and blue
9	(c) Differential stain	Haemolysis slight	Haemolysis very marked	Haemolysis slight	Haemolysis marked

TABLE IIIb.—REACTIONS.

No.		<i>Streptococcus</i> , diploid form (the organism easily associated with the symptoms described in text)	<i>Diphtheria</i> of <i>Dudgeon</i>	<i>Streptococcus faecalis</i>	The staphylococci	<i>Streptococcus pyogenes</i>	<i>Streptococcus urethrae</i>	<i>Streptococcus urethrae</i> (Pfeiffer)	<i>Streptococcus solitarius</i>	<i>Streptococcus salinarum</i>
1	Litmus milk—acid ?	+	+	+	+	+	Slight	...	+	+
2	Litmus milk—decolorized	+	+	...	-	...	-	...	-	...
3	Litmus milk—clot	-	±	+	-	-	-	-	+	+
4	Neutral red broth (anaerobically)	+	±	+	-	-	+	...	+	+
5	Saccharose ...	+	+	+	+	+	+	...	+	+
6	Lactose ...	+	+	+	+	+	+	±	+	+
7	Raffinose ...	+	±	-	-	-	-	±	-	-
8	Salicin ...	+	+	+	-	±	+	...	+	-
9	Mannite ...	+	+	+	±	+	+	...	72 hrs. +	-
10	Inulin*	-	-	...	-	72 hrs. +	-
11	Glucose ...	+	+	...	+	+	+	...
12	Dextrin ...	+	+	...	+	...	+	...
13	Lævulose ...	+	+	...	+	...	+	...
14	Galactose...	+	+	...	+	...	+	...
15	Maltose ...	+	+	...	+	...	-	...	+	...

Pathogenicity not investigated—Dudgeon's and Pfeiffer's negative.
Agglutination tests also not investigated.

* Discarded owing to unreliability.

A Comparison between the Division Figures induced in Lymphocytes by Auxetics with the Jelly Method and the Mitotic Figures seen in these and other Cells in Sections of Tissues by the Older Methods.

By H. C. Ross.

At the meeting of the Section held at the Lister Institute on November 7, 1911, a demonstration was given by us of the fixed specimens, photographs, and of a few stained living specimens of lymphocytes in the act of cell-division induced by auxetics.¹ A paper² on this subject was read the same evening by Sir Ronald Ross, in which he described the division figures as he had seen them both in the living state (demonstrated to him by us) and in the fixed films. He pointed out that there is strong evidence to show that the figures were those of cell-division, and stated that in his opinion there is no question that white blood cells can be made to divide in response to auxetics. At the subsequent discussion some gentlemen intimated that from what they had been shown they were not convinced that the figures were those of cell-division, because the latter were not exactly like the mitotic figures with which they were conversant from the observation of mitosis in fixed sections of tissues. These gentlemen, of course, have not had the opportunity of making a prolonged study of the induced divisions in cells, stained alive by the jelly method, as we have. To Sir Ronald Ross, on the other hand, we have had the privilege of demonstrating a considerable number of living division figures, in addition to submitting to him all the fixed films of them in our possession, and therefore he was in a position not only to discuss the pros and cons of the question, but also to contrast what he had recently seen with the normal resting blood cells with which he was so well acquainted by his many years' work with the parasite of malaria. But even Sir Ronald Ross has not had the opportunity of seeing as many of the division figures in all their phases as I have seen, and for this reason I now propose to discuss in more detail the comparison between the induced figures in lymphocytes and the

¹ A detailed description of this work will be found in former publications.

² Vide *Proceedings*, p. 103, and also *Nature*, December 14, 1911 (abstract).

appearance of cells found in the act of division by the older methods. I may add that the same objection has been raised in America and elsewhere.

At the outset attention may be drawn to the following points. Hitherto the phenomenon of mitosis has been studied almost entirely by the observation of cells found in the act of division in sections of tissues which have been fixed and stained by the usual processes. Until divisions were induced in lymphocytes by the jelly method, individual cells have not been watched going through the phenomenon of mitosis from start to finish, with their morphological elements distinguished by differential staining. Cells have been seen in the resting stage, and cells have been "caught" in the various stages of mitosis; comparisons have been made between the various stages, and between the stages and the resting cell, and it has been *deduced* that this morphological element in the several phases is derived from that morphological element in the resting cell, and so on. These deductions are undoubtedly correct for the majority of cells, and, owing to this fact, hard and fast rules have been made; indeed, these rules have become so firmly established that, unless one can show that the induced figures, which we assert to be mitotic figures, conform exactly to the accepted pictures, critics are inclined to dispute that we are dealing with mitosis at all. It is important to realize that, while many classes of cell appear to be identical morphologically, we have no right to accept the statement that a certain structure in a given class of cell is necessarily the same structure in another class of cell, merely because it looks the same and appears to have the same relations to other structures. As I have said before, I do not think that we are justified in taking for granted the nature of cellular elements until we have witnessed the whole life-history of the cell in question. Undoubtedly, in the main principles, when they divide by mitosis, cells seem to adopt a common method of reproducing themselves, but in the details of the division figures differences are frequently apparent. In cytology, especially in the cytology of blood cells, speculations have been rife, sometimes emanating from the highest sources, and in many instances they have been universally accepted without a murmur, as such theories appear to meet the case.

Another point is that, owing to the usual teaching of cytology, one is apt to get into the habit of thinking that cells when they divide do so in definite stages or phases, into which, for convenience of description, the phenomenon of mitosis has been divided. It is not many years ago

that in many cases the only details about cytology which students were taught were brief descriptions of the aster and diaster pictures of karyokinesis. The well-known diagrams of these stages were shown them, and I have actually found that some persons, when we are inducing cell-division, seem to expect one to make a living dividing cell always resemble one or other of these diagrams. Cells do not conveniently dwell in the prophases, metaphases, anaphases, or telophases. Mitosis is largely the phenomenon of the "shuffle" of the chromatin, so that each daughter cell may receive a due share of the hereditary characteristics; it is a sedate process which goes on steadily without any pause during cell-division. In living cells one frequently sees this shuffle taking place satisfactorily, although the figures appear to be atypical. The so-called phases of mitosis are arbitrary, arranged by cytologists. They are very convenient, and I believe that they have been so arranged because, by the fixation methods, large numbers of cells have happened to have been found in the act of presenting one or other of them. When one is inducing cell-division, however, one does not necessarily have the same fortune, and it is the exception rather than the rule to see cells presenting one or other of the well-known phases, which nowadays are nearly always only diagrammatically represented in books on cytology. It is a matter of chance whether one sees cells in this or that well-known phase. In reality the probabilities are against it, and if a section of a tissue is looked at critically one may frequently see more cells in a transitional stage between two of the so-called phases than actually in the phases themselves. Unfortunately, it is not common for specimens to be examined thus critically; one usually examines a section of a tissue with a comparatively low power, casually passing field after field in front of the objective. If a *typical* mitotic figure appears, it immediately arrests attention because it is so familiar, but figures not in the well-known phases are apt to be passed over. Hence people become inclined to consider that unless cells present some conventional picture of mitosis, the latter are not undergoing the phenomenon of indirect cell-division.

The question of trying to convince people, which was raised at the meeting, is almost entirely a question of being able to produce records of one's work. Others, of course, want to see the division figures for themselves, and this has proved to be the most difficult part of our researches. In order to do it there are three courses open at present. One is to repeat the experiments in the presence of others, and to try to get some good specimens of division figures in the

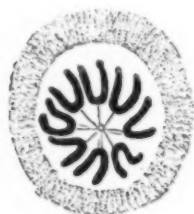
living cells. Another is to take photographs of the living cells in the act of division (which we did, and for reasons already given¹ proved to be most unsatisfactory); and the third method is to fix some specimens of the dividing cells in the way described in our last publication,² and to show the fixed films. I have already described in both of the former publications the difficulties which attend the demonstration of the divisions in living cells to large numbers of people. The cells do not live long, and soon become achromatic. Several fields may have to be searched through before good specimens are found, which involves delay, and perhaps disappointment. Even the living cells frequently appear distorted owing to the fact that they are pressed out between the jelly and cover-glass, and until one happens to have seen an undistorted specimen it is hard to believe that the distorted ones have any relationship to mitosis. It is not very satisfactory to demonstrate the figures in the living cells unless our critics are prepared to spend many hours with us searching through large numbers of fresh films, and patiently waiting until a series of figures are seen. We have found that onlookers are seldom prepared to do this.

With regard to the fixed films, however, there are hopes of ultimately obtaining a set of specimens of the induced division figures in all their phases. I do not assert that we shall be able to do this ourselves, because we hardly feel justified in devoting all our time, perhaps for months to come, in trying to get records of facts about which we are absolutely certain, and of which we now have confirmation by other procedures; but it is to be hoped that others will gradually try the jelly method and the fixation of the films, when a series of typical figures may be obtained for permanent record. The probabilities are that a very large number of films will have to be made, for in each jelly film from which the fixed specimens are prepared the majority of cells may be distorted. There may, of course, be one or two typical figures, although even then the chances are that they may not be absolutely in a definite well-known phase of mitosis, and even if they are in one of the stages, the attitude (over which there is no control) which they present to the observer may not be suitable. Supposing there is one such cell, however, it may not ultimately be fixed to the cover-glass, for during the process of fixation it may become achromatic and disappear, or it may, as many of the cells do, adhere to

¹ "Induced Cell-reproduction and Cancer," 1910.

² "Further Researches into Induced Cell-reproduction and Cancer," 1911.

the jelly and not to the cover-glass on the removal of the latter. Again, it may not be in the zone of fixation at all, because, as already shown, the fixing osmic acid only penetrates a certain distance under the cover-glass. Furthermore, supposing that a film did contain a typical figure, the latter can easily escape observation. One can never be certain of examining every field, especially as high powers have to be used, and it is very easy to lose a cell again in spite of the fact that one's microscope is fitted with accurate verniers. There is no question that, if we are going to obtain records of lymphocytes with division figures induced in them resembling all the well-known phases of mitosis, we shall have



From Gray's "Anatomy."



From a diagram of chromosomes in *Ascaris* egg. Wilson's "Cell in Development."



A dividing lymphocyte in a fixed film (polar view). From our "Further Researches into Induced Cell-reproduction and Cancer," vol. i, September, 1911, p. 38, fig. III.¹

to be blessed with extraordinary good fortune, unless many thousands of films are made and critically examined. I may mention that it occupied a whole year's work for two of us to obtain the photomicrographs of dividing cells which we have published, and none of them are either typical or satisfactory. In the fixed specimens which we have already obtained, however, there are some good figures, which, although they are not actually in the conventional phases, are sufficiently close to one or other well-known stage that one can, I think, after having seen the living cells in all their stages and attitudes, as I have done, show their

¹ Fig. 5 in "Further Researches into Induced Cell-reproduction and Cancer," vol. i, is a painting of another cell in a fixed film in almost precisely the same stage as this one.

relationship to the phases and point out the sequence of events. I will deal first with the four figures painted from the fixed films and reproduced in colours in our last publication. They are the most typical permanent specimens which we have obtained up to the present.

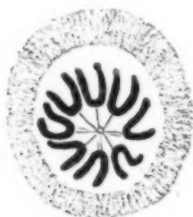
Before comparing the figures I wish to reiterate that the induced division figures of lymphocytes resemble mitotic figures except that the chromosomes are formed, not from the chromatin "ids" within the nucleus, but from the chromatin granules, which, in these cells, are immediately outside the so-called nucleus and in the cytoplasm.

We may begin by comparing the best of our recorded figures, that of a polar aspect of mitosis in a fixed film (illustration No. III in "Further Researches, &c."), with diagrams of similar aspects in Gray's "Anatomy," and in "The Cell in Development and Inheritance," by E. B. Wilson (*see opposite page*).

At first sight there appears to be no similarity between Wilson's or Gray's diagrams and our own illustration of the mitotic figure in the fixed lymphocyte. Both of the former are diagrams of cells in the metaphase, polar view, and both of the cells are in a slightly later stage of mitosis than the lymphocyte, which is a transitional stage between the late prophase and early metaphase. As I have seen exactly how the chromosomes are formed in the lymphocyte, it is easy diagrammatically to place our illustration in a slightly later stage, namely, in the metaphase. As the illustration is that of an early figure, the internal ends of the loops or festoons appear to meet at the centre of the cell, which in reality is the pole of it, or position of the centrosome. The continuation of the loops is due to the fact that not quite all the granules (ids) have yet collected at the equatorial plate ultimately to form the chromosomes, and some are still on their way, extending down in the grooves of the "spindle," which, of course, is somewhat flattened out owing to the fixation. Hence, when we now draw the cell in a later stage, these meeting lines must not be complete. Each loop or festoon divides transversely at its centre at the place indicated by the black lines in this diagram:—

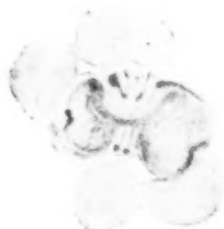


We may now compare once again the diagrams of Gray and Wilson with our figure in which the loops are divided to form chromosomes,



thus depicting the cell in its early metaphase. As in Gray's and Wilson's diagrams, the chromosomes are V-shaped, attached at their apices to the spindle, which, of course, is unstained.¹

Thus, by converting the illustration of the fixed lymphocyte diagrammatically into a slightly later stage of mitosis, one can show how the chromosomes do to some small extent resemble those in the well-known diagrams.



A dividing lymphocyte in a fixed film (profile view). Fig. II, "Further Researches into Induced Cell-reproduction and Cancer," vol. i.

With regard to the profile aspects of the division figures, figs. II and IV in "Further Researches" depict cells which are in a transitional stage between the metaphase and telophase. As a matter of fact the cells are in the telophase, but they both show a few chromosomes still remaining at the equatorial plate (metaphase) which have not yet dispersed into the daughter cells.

In reality, therefore, this figure is an "intermixture" of two phases, examples of which are depicted by Wilson's diagrams.

¹ If the same procedure is adopted with fig. V in "Further Researches into Induced Cell-reproduction and Cancer," vol. i, a very similar result will be obtained.

We can alter our figure diagrammatically, in a way similar to that adopted with the polar aspect figure, for, by deleting some of the ids on the one hand and the chromosomes on the other, we can show the same figure in the metaphase (or early anaphase) and in the telophase.

Our profile figures are all, of course, in a much later stage of mitosis than the polar view ones which we discussed first. For this reason the so-called nucleus in the profile figures appears to be stained. In the polar view figures, practically all the chromatin granules have collected

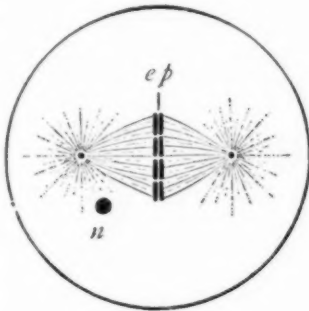


FIG. 26g.
Metaphase.

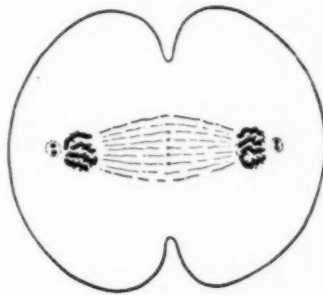
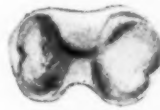


FIG. 26i.
Telophase.

From "The Cell in Development and Inheritance."



Metaphase (or early anaphase).



Telophase.

at the equatorial plate, because the cells are just entering the metaphase. As already described, a few ids still remain in lines radiating from the pole to the apices of the chromosomes, or rather of the loops which will ultimately form the chromosomes. Hence the nucleus or spindle is practically colourless. In the profile figures, however, the cells are leaving the anaphase and entering the telophase; a few of the ids still remain as chromosomes, but the majority of the chromosomes have broken up again into ids, which have become distributed over the surface of the daughter "nuclei." During the process of fixation

Fig. 1 is a diagram of a resting lymphocyte. The so-called nucleus, studded all over its outer surface by granules, may be noted. These ids, judging by the way they stain with aniline dyes, are composed of chromatin. They are in the cytoplasm, and are frequently seen to be extruded into pseudopodia. Within the nucleus is the ring-shaped nucleolus.

Fig. 2 shows a cell in the earliest prophase. It is slightly elongated, and the nucleolus has divided into two parts which are diverging towards the poles. The ids are comparatively deficient at the poles, owing to the fact that they are beginning to collect in the neighbourhood of the equatorial plate.

In fig. 3 the same condition is more marked, and the so-called nucleus is spindle-shaped. The nucleoli have adopted the positions of centrosomes. A few ids can still be seen extending downwards in lines from the poles to the equatorial plate, where the majority of them have collected.

Fig. 3a is the polar aspect of fig. 3. The radiating lines of ids can be seen resembling those in fig. III in "Further Researches" (see page 176).

Fig. 4 shows a slightly later stage. The ids have become more consolidated, both at the equatorial plate and in the lines where they extended down to the poles, lines which are now no longer complete.

Fig. 4a shows how, when this stage is looked at from the pole, the ids have become arranged in indefinite festoons, semilunar-shaped, eight in number.¹

In fig. 5 the ids have collected to form what appears to be a solid belt of chromatin at the equatorial plate.

Fig. 5a is the polar view showing that, owing to the festooning, the belt has a rosette arrangement.

Fig. 6 is the first step in the metaphase. Each festoon has divided transversely at its centre, but for the present each half thus produced remains united at its end with the end of half of its fellow-festoon.

Fig. 6a shows this more clearly, and it may be compared with our diagrammatic alteration of fig. III in "Further Researches" (see p. 178). This transverse splitting of the festoons leaves the figure with eight V-shaped chromosomes, having their apices inwards attached to the nucleus spindle.

Fig. 7 is the first one of the anaphase. The V-shaped chromosomes have divided at their apices.

Fig. 7a, the polar view, now depicts the cell with the chromosomes divided into sixteen portions.

Fig. 8 shows each portion gradually travelling towards a pole—eight to one pole and eight to the other. (As the diagram is of a longitudinal section, only half this number appears in it.) While they travel the rod-shaped bodies break up again into ids, thus reverting to their resting condition.

Fig. 9 is a later stage where the ids are diffusing over the surface of the daughter "nuclei," which are formed from the spindle. The latter has become constricted at its centre.

Fig. 10 is a diagram of the telophase. The daughter cells are formed and about to separate. The centrosomes have become invaginated within the "nuclei."

In fig. 11 complete division has occurred. The chromosomes have entirely reverted into ids, which once more cover the surface of the so-called nucleus. The centrosome again appears as the nucleolus.

¹ Throughout these diagrams the number of festoons, and therefore of chromosomes, is eight, which is commonly seen. In the induced figures, however, sixteen and thirty-two chromosomes may also be seen.

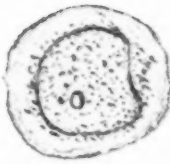


FIG. 1.



FIG. 2.



FIG. 7.



FIG. 7a.



FIG. 3.



FIG. 2a.



FIG. 8.



FIG. 4.



FIG. 4a.



FIG. 9.



FIG. 5.



FIG. 5a.



FIG. 10.



FIG. 6.



FIG. 6a.



FIG. 11.

these chromatin granules have become flattened out and crushed into the daughter nuclei, giving the latter the appearance of being composed of deeply and more or less homogeneously staining chromatin. If a fixed lymphocyte is stained in its resting stage, the so-called nucleus appears to be a deeply stained chromatin mass, but if a living resting lymphocyte is stained by the *in vitro* method, as already described in former publications, the so-called nucleus appears as a transparent membrane with no chromatin inside it, but studded all over its outside by minute chromatin granules.

It is unfortunate that it is so difficult to obtain records of the cells with the induced division figures in them, because otherwise I feel sure that many persons would try the new methods, and see for themselves how the cells divide, rather than rely too implicitly on the conventional diagrams of cytology. We have done our best to obtain what records we can, but it is tedious work which only delays progress. One must admit that our records are poor, and it is not surprising that people ask for something better. Unless some remarkable new method of recording the specimens is invented, I think that the quickest way to overcome the difficulty is for those who are interested to employ the jelly method for themselves. Hitherto I have purposely refrained from trying to establish the induced figures by means of diagrams, because I considered that it was useless to expect people to believe in mere drawings when the subject of the induced division of human cells is so new. For this reason we resorted to every means in our power to obtain actual records of the cells themselves; but it is now two and a half years since the divisions were first induced, and although every effort has been made to obtain as many records as possible, it must be admitted that the results are not so satisfactory as one could wish. It is possible that if we went on for another two and a half years, while the chances are that we should get slightly better records, we might not meet with more success, and our specimens and photographs remain as unconvincing as before. Therefore, I now propose to describe with the aid of diagrams the division of human lymphocytes induced by auxetics as I have seen them, stained *in vitro*, but it should be remembered that they are only diagrams, drawn from memory, and that we have no fixed specimens like them all.

In order to demonstrate the relative position of the structures, in all these diagrams the so-called nucleus has been more clearly outlined than is really the case. (Figs. 1 to 11, p. 181.)

Such is the manner in which lymphocytes divide. The figures are

similar to mitotic figures except that the chromosomes are formed from the granules which are immediately outside the so-called nucleus. This point at first appears to be very revolutionary, but there is no doubt that the nature of the granules differs sometimes in different classes of cells. For instance, the granules of liver cells are quite different and stain differently from those of lymphocytes and leucocytes. Yet these granules, in many classes of cells, have all been heaped together under the common name of "Altmann's granules," and some people expect them all to have the same function. We have no proof that these structures in all classes of cells are derived from the same source, any more than we can assert that the structure known as the nucleus in one class of cell has necessarily the same function as that which is known as the nucleus in another cell until we have witnessed the life-history of both classes. Take the case of the so-called polymorphonuclear leucocyte. Wharton Jones in 1846 first stated that these cells were "nucleated." He suggested that the curious shaped body within these cells was the same thing as the nucleus in other cells except that it was polylobed. He had no grounds whatever for his statement, which really was in the nature of a speculation. But it was jumped at and accepted, and, although the cells had never been seen to divide, they were given the name of "polymorphonuclear leucocytes." Now that we can make these cells divide, and dispute the accepted idea of their so-called nucleus, we are attacked on all sides. I presume that the word nucleus originally meant a body inside another, but this is no criterion that all nuclei should have the same function.

Intranuclear centrosomes have been seen in other cells as in lymphocytes, and I have been informed that some of the spindle fibres in some cells appear to be formed partly out of the nuclear wall. Only recently, in a paper reported in *Nature*,¹ the author points out how during mitosis in certain cells, the nuclear wall shrinks and envelops the chromosomes. It is possible that the appearance of the spindle fibres may partly be due to some post-mortem effect. I have never seen them in a living cell, although our fixed films show some lines indefinitely resembling them.

Critics have suggested that lymphocytes are sometimes found in the act of division in sections of lymphatic glands, and we have been asked why our figures do not resemble them. But if these sections are not stained too deeply, and some resting lymphocytes in them very carefully compared with the mitotic ones, it may be seen that the chromosomes

¹ See *Nature*, November 9, 1911, p. 59. As far as can be ascertained, this paper has not yet been published in full.

are formed out of the granules. It is as well to ask oneself as to what has happened to the granules in the dividing cells in the sections, for they no longer appear to be visible. In reality they have formed the chromosomes.

In conclusion, I should like to take the opportunity of mentioning experiments which show that the division of white blood cells does not appear to depend on alterations of surface tension. We have been asked about this point on several occasions. Jellies have been prepared which have contained different strengths of sapolin, sodium glycocholate, sodium taurocholate, and oleic acid, and their action tested on the living cells in precisely the same way in which we test auxetics. With none of them has any action been visible, except that if they are present in strong solution they burst the cells. They do not excite amoeboid movements (kinetic action), and they certainly do not induce division figures.

It may be mentioned that while this paper was in the press, by means of a series of experiments, cell-divisions have been induced in the ova of *Ascaris megalocephala* by the agency of the auxetics which induce the cell-division of lymphocytes and other human cells. The auxetics employed were extracts of dead tissue, creatine, &c., and they rapidly induce development and cell-division through several generations in the unfertilized eggs. This is important confirmation of the fact that the figures in lymphocytes are division figures.

DISCUSSION.

Dr. E. F. BASHFORD said that when last the subject of Dr. Ross's paper came before the Section he had endeavoured to offer some serious criticism to which he had nothing to add.

Dr. J. A. MURRAY disagreed entirely with the description of the process as mitosis. He pointed out that the chromosomes had been seen in living amphibian cells by dark ground illumination, and that Boveri had figured the centrosomes in the blastomeres of *Ascaris* as refractile spheres outside the nucleus, the latter being still bounded by the nuclear membrane. Dr. Murray thought the process might be regarded as an amitosis of cells in the dying condition, and the metachromatically staining structures, which the author identified as "chromosomes," he regarded as part of the mitochondrial apparatus, analogous to the "Nebenkern" of snail spermatocytes, which stain in the same way with methylene blue in the living condition and undergo a mass division during mitotic cell-division.

Dr. Ross replied that he had only described the division figures induced in lymphocytes, but did not dispute the origin of the chromosomes in some other classes of cells. With regard to the suggestion that the cells were merely undergoing division in a dying condition, it appeared to him that it was rather futile for cells to undergo division while in the dying state: and he pointed out that recently not only had division been induced by auxetics in *Entamoeba coli* but also that these parasites had been cultivated through six generations without transplantation, entirely by the agency of those substances.

A Case of Ulcerative Endocarditis produced by the Pneumococcus in a Child, aged 3.

By H. R. DEAN.

THE patient was a female child, aged 3. She was said to have been always a weakly child. The illness began with vomiting on January 14. On the next day she was drowsy, but screamed if roused. On January 16 she was admitted to the Victoria Hospital for Children under the care of Dr. A. C. D. Firth. The typical signs of meningitis were present. The patient died on January 17.

Post-mortem examination: The body was poorly nourished. A well-marked purpuric eruption was present on the skin of the thighs and shins. The individual petechiæ were small, round, well defined, and of a purple colour. The pericardial sac contained a little clear fluid. The heart was large. Both ventricles were dilated and hypertrophied. Both auricles contained laminated clot. The clot contained in the right auricular appendix was adherent to the wall of the chamber. The right ventricle contained a large laminated clot which was adherent to the anterior wall of the ventricle immediately below the tricuspid valve. On removal of the clot an area of superficial ulceration was found. Numerous vegetations were present in the space between the infundibular segment of the tricuspid valve and the wall of the ventricle. There were no vegetations on the internal surface of the segments of the tricuspid valve. The mitral valve was thickened. One large and several smaller patches of granulations were found on the anterior segment of the mitral valve. The left ventricle contained a laminated clot which was adherent to the mitral valve. The aortic and pulmonary valves were normal. The lungs were extremely

congested and œdematous, but there was no sign of consolidation. The peritoneum was reddened and injected throughout. The liver was large and on section presented a typical fatty nutmeg appearance. The spleen was large and firm. The kidneys were of normal size, of a tough consistence and a deep red colour. Neither liver, spleen, nor kidneys, contained infarcts. The vessels of the stomach and small intestine were distended. On removing the skull-cap the surface of both hemispheres was found to be covered with a thick layer of greenish pus. Thick pus coated the base of the brain involving the origins of all the cranial nerves. The cerebral vessels were examined for embolism without success. The substance of the brain was extremely soft, but there were no localized collections of pus. Sections of granulations on the tricuspid valve showed a few clumps of pneumococci. Sections of the liver showed a condition of extreme passive congestion with well-marked fatty change.

Bacteriological examination: A specimen of the cerebrospinal fluid was removed during the life of the patient. It contained large numbers of pus cells and pneumococci. At the post-mortem examination specimens of the heart-blood were taken before the heart was opened. Pneumococci were present in the films made from the heart-blood, and the pneumococcus was obtained in pure culture. Numerous pneumococci were found in films made from the pus obtained from the surface of the brain, and a pure culture of the pneumococcus was obtained from this source. The cultures of the pneumococcus were of typical appearance and killed inoculated mice in twenty-four hours.

The interesting features of the case are the age of the patient and the distribution of the lesions on the right side of the heart. The lesions were undoubtedly due to the pneumococcus, and at the post-mortem examination the lungs showed no evidence of bronchopneumonia. Judging by the state of the ventricular wall and the appearance of the liver, it seems likely that valvular disease had been present for some considerable time. Indeed, chronic valvular disease may well have been present before the onset of the final infection. In any case it seems quite certain that the suppurative meningitis was secondary to the heart condition.

I am indebted to Dr. Firth for his kindness in allowing me to make use of the clinical notes of the case.

Pathological Section.

March 19, 1912.

Dr. R. T. HEWLETT, President of the Section, in the Chair.

An Improved Method for Opsonic Index Estimations, involving the Separation of Red and White Human Blood Corpuscles.¹

By CHARLES RUSS.

THE opsonic index was introduced in 1905-06 by Sir A. E. Wright. It was for a few years extensively practised, but has fallen largely into disuse owing to its unreliability, which was realized by the profession, who were doubtless much influenced by the criticisms published by Mr. Greenwood and Dr. White, Dr. Hort, and others. In view of the value that an accurate method would possess in clinical work it seemed well worth considerable study, if the large liability to error could be removed, or at least reduced.

Opsonin is the name given by Sir A. E. Wright to the substance in human blood which is understood to cause the ingestion of bacteria by the leucocytes, and since this varies quantitatively in health or disease it is important that we should be able to measure its fluctuations in any patient's blood, its increase favouring recovery from the infection, and its deficiency assisting the disease.

In the opsonic test or estimation, leucocytes are set to ingest bacteria when mixed and incubated with normal serum, and the same operation is conducted with a diseased serum under similar conditions. In stained

¹ The main features of this work were conveyed to the Royal Society in a paper read March 14, 1912.

films the bacteria visible in, say, fifty of such leucocytes are counted in each case and the figures so obtained are contrasted. This ratio is used as a measure of the amount of opsonin in the two specimens of blood serum. The healthy serum is taken as the normal or control, and the diseased may of course be found to contain more or less, or the same—i.e., a normal amount of opsonin to the bacteria used, which may be any pathogenic organism.

From variations in the opsonic index of the serum of patients suspected of tuberculosis numerous diagnoses of tuberculosis have been made, and infection by certain other bacteria has also been presumed by opsonic comparisons on similar lines. Since opsonin has not been separated from the blood and we have no colour or simple test for its presence, the only practical method of its measurement at present available is this opsonic test or index.

Dr. Hort took a large sample of a patient's blood, divided it into several smaller volumes, disguised the identity of the specimens and obtained the opsonic index to the tubercle bacillus from several different operators simultaneously, at different pathological laboratories. These operators also measured the opsonic index of two sera which they did not know were identical. The results were discordant, and may be reviewed by reference to his paper.

Mr. Greenwood and Dr. White studied the mathematical liability to error arising from the method of counting the bacteria in a random sample of the leucocytes, instead of counting those in all of the leucocytes employed in each mixture (the accurate, but impractical course, on account of the labour involved). Since my work has followed the line of weakness indicated by him, it is necessary to give the important points of his work. If, for example, in any count 200 bacteria have been seen in the fifty leucocytes, it must be remembered that each leucocyte does not contain four bacteria, but their content is any number from 0 to about 25 or more, a series of numbers being added. Now, when a film is made in which the leucocytes contain all these varying numbers of bacteria, there is a great liability that the blanks (0 contents) and high contents (gluttons) are distributed unevenly in the film. Therefore, according as the operator begins counting in part of the field rich in one type of leucocytes or the other, the figure he will obtain will be a low or high one; the most significant point.

In their first communication Mr. Greenwood and Dr. White (R¹) concluded from a study of films prepared in Sir A. E. Wright's laboratory that the distribution of leucocytes (arranged with respect

to the number of ingested tubercle bacilli) is highly asymmetrical and surmised that the variations from the mean value, exhibited by samples of fifty or twenty-five, of the whole "population" of cells would be considerable. In the second paper (R) they analysed a count of no fewer than 20,000 leucocytes upon films prepared and counted by Dr. White. After elaborate mathematical analysis they concluded that a serum having precisely the same opsonic content as the standard might be expected once in seven trials to yield an index deviating from unity by as much as 33 per cent. in either direction. From this and further calculations they concluded that even in the case of samples of 100 it is doubtful whether single determinations which give values even beyond the limits of 1.3 to 0.7 can be regarded as satisfactory evidence of differentiation.

In the experiments I am about to detail, I had the valuable assistance of Dr. Cavendish Fletcher far into the exploratory stage, but unfortunately he had to abandon the work. The first idea was not directly associated with the error emphasized by Mr. Greenwood. It may be expressed as follows:—

Since the leucocytes act in the opsonic mixture as bacterial magnets, then if in the two mixtures there were very different numbers of them at work, this difference might cause a variation in the degree of phagocytosis in the two cases, apart from variations in opsonin. To test this point, the opsonic estimation was made of a sample of normal serum to the *Staphylococcus aureus*, and at the moment of withdrawal of the mixture from incubation part was withdrawn in a corpuscle-counting pipette, the remainder formed the films from which the ordinary opsonic figure was obtained by one worker and the other meanwhile counted the leucocytes which had been at work. This proceeding was repeated several times at a sitting with identical materials, and from four such sittings the results shown in Table A were obtained.

From this table the following points are apparent:—

- (1) There was a considerable variation in the number of leucocytes obtained by successive dips into the vessel containing the "washed" corpuscles.
- (2) This variation showed no definite association with a high or low figure obtained by the corresponding opsonic count.
- (3) The opsonic figure obtained was liable to marked fluctuation, though it should have been constant, since all the materials were identical and the operator the same.
- (4) There appeared to be the all-important constancy of the opsonic

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figure when the numbers of blanks met during a fifty count was the same or nearly so.

TABLE A.—OPSONIC INDEX (OLD METHOD).

Repeated estimation of the opsonin to *Staphylococcus aureus* in normal serum and simultaneous enumeration of the leucocytes per cubic millimetre in each opsonic mixture.

Series	Leucocytes per cubic millimetre	Opsonic count per 50 leucocytes	Error above average	Error below average	Mean value	Blanks per 50 leucocytes	Worst error above average	Worst error below average
			Per cent.	Per cent.			Per cent.	Per cent.
1	1 15 × 200	279	26	4	292	9	15	—
	2 9 "	337		—		9		
	3 14 "	285		2		7		
	4 11 "	268		8		6		8
2	1 18 × 200	190	16	11	170	10	52	—
	2 16 "	258		52		3		
	3 19 "	118		30		20		
	4 10 "	114		33		20		33
3	1 14 × 200	185	23	8	170	16	25	—
	2 9 "	155		8		14		
	3 6 "	213		25		18		
	4 16 "	137		19		21		19
	5 36 "	180		5		13		—
	6 12 "	155		8		14		—
4	1 12 × 200	151	15	20	190	11	17	20
	2 7 "	191		—		7		
	3 25 "	194		—		8		
	4 10 "	224		17		4		
Corrected total			133	132				

Average error above or below the mean value ... $\frac{265}{18} = 14.7$ per cent.
Worst error above ... 52 per cent.
Worst error below ... 33 "

All the materials were identical in each series, and the opsonic estimations by the same operator, and the observations made at about half-hour intervals.

The numerator = the highest bacterial content of any leucocyte in the series.
The denominator = the number of times it occurred in the series.

This last feature suggested that this large content variation might be due to uneven access between leucocytes and bacteria. However, the outstanding fault of the process in this large variation in the leucocyte content and its occurrence could only be due to difference of (1) *Appetite* or (2) *Opportunity*, or a combination of these factors.

(1) *Appetite*.—If the leucocytes have equally as good chances to pick up bacteria in the opsonic mixture, and yet show this variation, it must be presumed physiological, and there is no remedy.

(2) *Opportunity*.—It may be that all the leucocytes have similar appetites, but get very different opportunities to pick up bacteria owing to uneven distribution of the mixture.

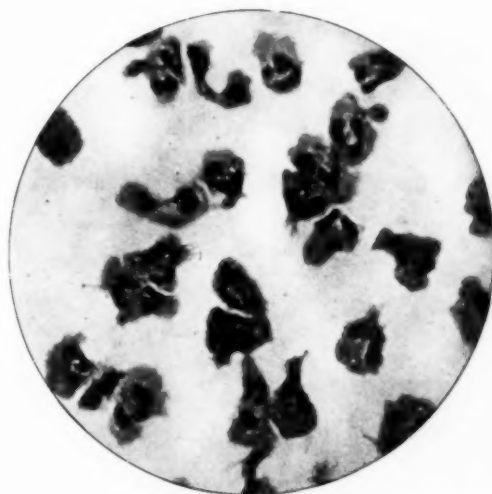


FIG. 1.

The polynuclear human leucocytes as seen on the plates of the "Ponder" cell, after washing the plate free of red corpuscles by saline. ($\frac{1}{2}$ obj.)

A scrutiny of the materials used in the old method showed two important defects:—

The Presence of Red Corpuscles.—Although white corpuscles only are concerned in the process, both red and white blood corpuscles are used; but since a bacterial suspension not exceeding 500 mm. per cubic centimetre is used, and washed blood corpuscles contain 5,000 mm. red, and 10 mm. white corpuscles per cubic centimetre, it is evident that for every leucocyte there are fifty bacteria provided; but surrounding this all-important leucocyte are 500 obstructing and useless red corpuscles. I therefore decided to abolish the red corpuscles, and this involved the separation of red and white human blood corpuscles.

The methods which were tried unsuccessfully included:—

Hæmolysis of the red corpuscles.

Agglutination by ferric chloride and filtration of the red groups.

Filtration of decalcified blood.

Sedimentation of decalcified blood after artificially raising the specific gravity.

However, Dr. Ponder's work on leucocytes furnished the nucleus of a successful method. He found that when blood is enclosed in a cell between two glass plates and incubated, there occurs a swarming of polynuclear leucocytes to the glass surfaces, to which they adhere firmly and appear remarkably distorted (fig. 1). My first problem was to get these leucocytes off the glass. This was found to be effected by citrate saline solution 1·5 per cent., 0·8 per cent. by di-sodium hydrogen phosphate, and by hypertonic salt solution and also by serum. After

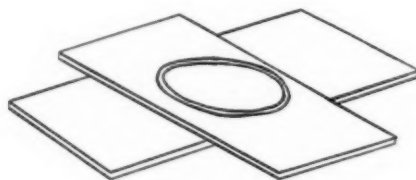


FIG. 2.

The modified "Ponder" cell, consisting of two glass plates, $1\frac{1}{4}$ in. by 3 in., enclosing a cell, bounded by an india-rubber ring—the latter being filled with freshly shed human blood, and of nearly 1 in. inside diameter.

obtaining a large number in a test-tube in the citrate solution (to make films), I found they were highly unstable osmotically, and when transferred to normal saline the majority burst.

After experimenting with over 200 Ponder plates I realized that the leucocytes could only be obtained in bulk if favourable chemical conditions were ascertained (since incubation aggravated the bursting). The following method succeeded in supplying a majority of polynuclear leucocytes (the lymphocytes do not appear on the plates) in good condition, which could be incubated for fifteen minutes as in the opsonic index process. The detailed method is as follows:—

Blood is shed into a rubber ring (cell) sandwiched between two glass plates (fig. 2). This cell is incubated for twenty minutes at $37\cdot4^{\circ}\text{C.}$, removed from incubation, the cell is opened, the clot and ring removed,

and the plates washed with 1.25 per cent. saline to free them from red corpuscles and serum. After wiping the ring margin clear of more red corpuscles and dried serum, a few drops of cold NaCl 1.25 per cent. are poured on the leucocyte-laden area of each plate. These are replaced on the metal shelf of the incubator for fifteen minutes; when the plates are inspected, the previously distorted and stretched out polynuclears will be seen under a low objective to have become almost spherical and loose from the plate. By means of a long glass rod the fluid and floating leucocytes are swept into a small tube and concentrated by the centrifuge at moderate speed. After syphoning off the supernatant

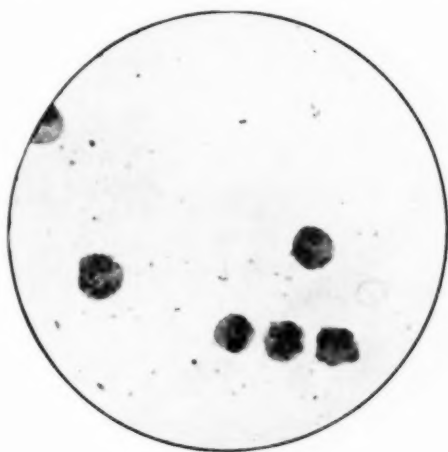


FIG. 3.

Human leucocytes (via "Ponder" plates) freed from red corpuscles, showing ingested staphylococci in opsonic process. ($\frac{1}{2}$ obj.)

fluid a very large number of human polynuclear leucocytes were obtained, 50 per cent. of which stand incubation with equal volumes of serum and the bacterial emulsion, the latter being made with 1.25 per cent. NaCl instead of normal saline (fig. 3).¹

¹ Since half of the corpuscles survive, those destroyed are potential obstacles to mixing and even phagocytosis. But the ratio is now one obstacle to one leucocyte, instead of five hundred to one when using ordinary blood. It is possible to get a somewhat higher percentage of good leucocytes by other means (detailed elsewhere), but since the technique is more laborious I use the simpler method.

But before proceeding to test the opsonic process for the anticipated increased accuracy, the second defect of opportunity in the *old* method had to be attended to. In the *old* method the opsonic mixture (serum, bacteria, and washed blood corpuscles) was incubated for fifteen minutes, but even at the end of ten minutes the bulk of the corpuscles had settled to the bottom of the glass pipette, the supernatant fluid being clear. Since equality of opportunity cannot exist when this is permitted, this defect was remedied by keeping the mixture in slow rotary motion during incubation by means of the opsonic mill (fig. 4).

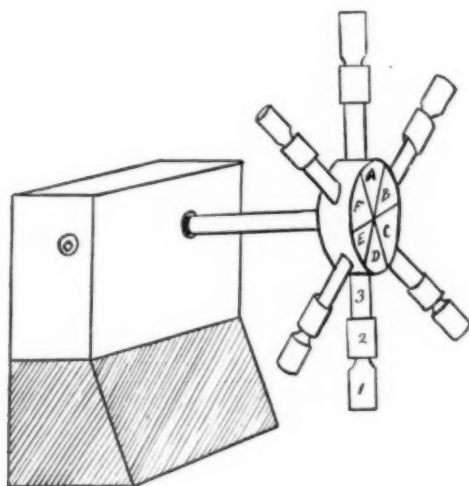


FIG. 4.

The Opsonic Mill. This clockwork-driven instrument, standing in the incubator, rotates the opsonic mixture and prevents sedimentation of the corpuscles. (Speed of rotation = one minute forty-five seconds per revolution.) 1, the shortened glass pipette; 2, india-rubber collar; 3, copper tube packed with fine copper wires.

A mechanism to prevent sedimentation of the opsonic mixture was devised by Rosenow (1906), and by Glynn and Cox (1912). The latter used a mechanism which rotated the pipette on its long axis in a horizontal plane, and their experiments showed no reduction of the error by its use when tested. Only a small benefit is to be expected from such an improvement, but it is probably inappreciable when the entire experimental error may be large, as in the old method. More-

over, their method of rotation is not ideal; for though sedimentation is prevented, there is no active mixing (from end to end of the pipette) induced by such a roller movement. In the device illustrated in fig. 4, not only does no settling occur, but experiments showed that the corpuscles pass up and down in the opsonic fluid during the changing positions of the pipette in the slowly moving wheel.

After a few trial experiments with the new materials I proceeded to test the opsonic index of the same serum repeatedly as in the experiments recorded (Table A), to ascertain whether the more even access and mixture of bacteria and leucocytes now improved the experimental error. The results are shown in Table B.

TABLE B.—OPSONIC INDEX (NEW METHOD).

Repeated estimation of the opsonin to *Staphylococcus aureus* in normal serum, using leucocytes only and the opsonic "mill." The series number indicates a set of four or six observations made at a sitting with the same set of materials.

Series	Opsonic count per 50 leucocytes	Error above average	Error below average	Mean value	Blanks	Worst error above average	Worst error below average
		Per cent.	Per cent.			Per cent.	Per cent.
1 Very thin bacterial emulsion	61	16	—	72	27	—	16
	72	—	—		17	—	—
	76	—	5		21	—	—
	79	—	9		19	—	—
	67	6	—		20	—	—
	84	—	15		14	15	—
2 Thin bacterial emulsion	117	—	13	103	13	13	—
	103	—	—		13	—	—
	114	12	11		12	—	—
	87	15	—		11	—	15
	91	11	—		10	—	—
	108	—	4		18	—	—
3 Medium bacterial emulsion	130	6	—	139	6	—	6
	147	10	5		9	5	—
	135	1	—		11	—	—
	144	—	3		8	—	—
4 Thick bacterial emulsion	160	10	—	178	4	—	10
	195	—	9		3	—	—
	197	—	10		6	—	—
	163	8	—		7	10	—
		74	84				

Average error above or below the mean ... $\frac{158}{20} = 7.9$ per cent.
 Worst error above the mean value ... 15 per cent.
 Worst error below the mean value ... 16 "

The results recorded in this Table (B) show a marked reduction of the average and maximum error from the mean value, and this had occurred in spite of a fairly wide variation in the strength of the bacterial emulsion used. Believing that still higher accuracy might be obtained, I undertook a further series of tests, matching the emulsion used in Experiment 3, Table B (which had been fixed by heat) as a standard. I also decided to count 100 leucocytes, fifty from each of the two films made from the mixture. The results are shown in Table C and show a still higher level of accuracy than those of Table B, though visual matching of the emulsions (to produce an average phagocytosis of three bacteria per leucocyte) was not very successful.

TABLE C.—OPSONIC INDEX (NEW METHOD).

Repeated estimation of opsonin in normal serum to the *Staphylococcus aureus*, using leucocytes only, and the opsonic mill, and counting 100 leucocyte contents.

Series	50 leuco- cytes. Film I	50 leuco- cytes. Film II	Opsonic count	Mean value	Error from mean value +	Error from mean value —	Blanks per 100 leuco- cytes	Maximum deviation +	Maximum deviation —
					Per cent.	Per cent.		Per cent.	Per cent.
1	144	105	249	10 256	—	2	18	—	2
	127	144	271		6	—	18	6	—
	107	146	253		—	1	16	—	—
	131	119	250		—	2	20	—	—
2	142	178	320	14 324	—	1	10	—	—
	170	159	329		1	—	15	—	—
	150	160	310		—	3	16	—	3
	176	162	338		4	—	8	4	—
3	127	120	247	14 252	—	2	49	—	—
	128	103	231		—	8	40	—	8
	144	113	257		2	—	32	—	—
	144	132	276		9	—	40	9	—
4	99	112	211	9 230	—	8	25	—	8
	114	144	258		12	—	19	12	—
	121	109	230		—	—	23	—	—
	96	125	221		—	3	25	—	—
					34	30			

Average error above or below the mean value ... $\frac{64}{16} = 4$ per cent.
 Worst error above 12 per cent.
 Worst error below 8 "

There was defective emulsification of the staphylococci in Series 3, evident in the "clumpy" films, but fortunately the entire results of the table can afford the handicap. All the films of Tables B and C have been preserved.

SUMMARY.

The improvements described have produced :—

(1) A striking reduction in the liability to error of opsonic estimations when repeatedly tested.

(2) The results recorded by the *new* method (Table C) showed a liability to error of about one-quarter the magnitude of those recorded in Table A (*old* method), the conditions of experiment being almost comparable.

(3) The enhanced accuracy is associated with a much reduced range of microbic content of the leucocytes (0—14).

(4) The improved results are attributable to the more even distribution of bacteria amongst the leucocytes (by the removal of the red corpuscles) and by its maintenance during incubation in the opsonic mill.

(5) No observations were made of any variations in opsonin in health or pathological states.

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The Bactericidal Action of Radium Emanation.¹

By HELEN CHAMBERS and S. RUSS.²

EXPERIMENTS have been made by several observers³ to find whether the rays emitted by radium have a bactericidal action. The general conclusion drawn from them is that these rays, especially those of the alpha and beta types, prevent the growth of certain bacteria. The bacteria under investigation in such experiments have been irradiated upon media in which they normally multiply. Although the general tendency of such observations rendered it improbable that the bactericidal action of the rays was really due to some effect upon the media, it seemed desirable to remove this objection, if possible. Experiments have accordingly been made by exposing suspensions of bacteria in distilled water to the various rays from radium. After irradiation, measured volumes of the bacterial suspension were planted on agar, and the number of colonies which developed compared with the number from an equal volume of the control suspension.

The organisms used in different series of experiments were *Staphylococcus pyogenes aureus*, *Bacillus coli communis*, *Bacillus pyocyaneus* and *Bacillus anthracis*. The main conclusion to be drawn from these observations is that the alpha and beta rays from comparatively small quantities of radium—i.e., a few milligrammes—have a direct bactericidal action.

It has previously been shown⁴ that the polymorphonuclear leucocytes of human blood suffer a reduction in their phagocytic power

¹ Read at the Laboratory Meeting of the Section, held at the Cancer Research Laboratories, Middlesex Hospital, on April 2, 1912.

² Beit Memorial Research Fellow.

³ Strebel, "Fortschritte auf dem Gebiete der Röntgenstrahlen," iv, p. 125; Aschkinass and Caspari, *Pfluger's Archiv f. die ges. Phys.*, Bonn, 1901, lxxxvi, pp. 603-18; Pfeiffer and Friedberger, *Berl. klin. Wochenschr.*, 1903, xl, p. 641; Hoffmann, *Hygienische Rundschau*, 1903, xiii, p. 914; Dixon and Wigham, *Dublin Journ. of Med. Sci.*, 1904, cxvii, p. 161; Goldberg, London (E. S.), "Das Radium in der Biologie und Medizin," Leipzig, 1911, p. 28 *et seq.*

⁴ Chambers and Russ, *Proc. Roy. Soc., Lond.*, 1912, lxxxiv, B, pp. 124-36.

and are eventually destroyed when exposed to alpha rays, also that the opsonin in normal serum is destroyed by these rays. With a view to some possible clinical applications of the bactericidal effects, a series of observations has been carried out, with known quantities of radium emanation, upon the destruction of three of the elements that enter into the process of phagocytosis—namely, leucocytes, opsonin and bacteria. The result of this investigation is that the destructive action of the rays upon the bacteria, in this case *Staphylococcus pyogenes aureus*, is much more marked than upon the two other constituents.

METHODS OF EXPERIMENTS UPON BACTERIA.

The method by which the bactericidal action has been studied is as follows: the growth is removed from a twenty-four hours' agar culture and centrifugalized in 10 c.c. of sterile distilled water to wash the organisms. The fluid is pipetted off and 3 c.c. of fresh distilled water added to the bacterial deposit, which is then well shaken. About 2 c.c. of this emulsion are run into a small glass bulb (volume usually 10 c.c.) provided with two taps and containing a measured quantity of radium emanation; the remainder of the emulsion serves as the control. The two emulsions are then placed in the ice-chest at about 4° C.

The emanation is partially dissolved by the emulsion. The solubility co-efficient for distilled water at 0° and 76 cm. pressure has been determined by Boyle¹ and found to be 0.51. Hence if the concentration of the emanation in the air within the bulb were 1 milli-curie per cubic centimetre² it would be about 0.5 milli-curie per cubic centimetre in the emulsion. The concentrations recorded in the paper refer to the number of milli-curies divided by the volume of the bulb. Throughout the fluid the bacteria are subjected to the alpha, beta and gamma rays from the emanation and its short-lived products, RaA, RaB, and RaC.

After any desired intervals a measured volume of the emulsion is withdrawn from the bulb and planted upon an agar slope, the same volume of the control being planted for comparison.

A series of tubes having been prepared in this manner for different times of exposure, they were incubated at 37° C.

¹ Boyle, *Phil. Mag.*, December, 1911.

² One milli-curie is the amount of emanation in equilibrium with 1 mgrm. of pure radium.

Staphylococcus pyogenes aureus.—The bactericidal action of the emanation upon this organism may be seen from fig. 1. The number of colonies gradually diminishes and eventually the fluid is sterile. The concentration of emanation in this series was 0.5 milli-curie per cubic centimetre. The control emulsion contained 3×10^9 organisms per cubic centimetre. It will be seen from the gradual diminution of growth that a completely lethal effect was obtained after five hours. As portions of the irradiated emulsion were removed from the bulb at various intervals for the above series, simultaneous observations were made upon stained films. The organisms showed no difference in their staining power after

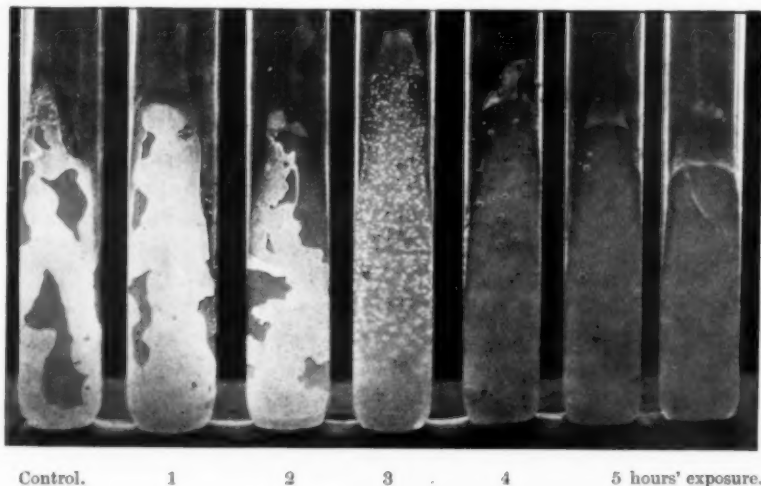


FIG. 1.

Action of radium emanation on *Staphylococcus pyogenes aureus*.

irradiation. After several hours agglutination had occurred. With more prolonged exposure this effect was sufficiently marked to be seen by the naked eye. The emulsion, originally neutral to litmus, gradually became acid. When the exposure had lasted sufficiently long for a completely lethal action, the emulsion was removed from the bulb, and in order to see whether the fluid, acid in reaction, had any direct lethal action upon the organisms, it was centrifugalized and the

clear supernatant fluid pipetted off. One volume of this fluid was added to an equal volume of the control emulsion and allowed to remain at room temperature. A control was provided by mixing one volume of the emulsion and one volume of distilled water. No agglutination was caused by the acid fluid. After twenty-four hours equal volumes from the two tubes were planted and incubated. The growth was in each case copious. After three days equal volumes were again planted and no difference in the two growths was detected. This indicates that the lethal action upon the organisms is a direct one, and is not to be attributed to changes in the fluid as a result of the irradiation.

Bacillus coli communis.—Emulsions of this organism in distilled water were exposed to the emanation, and the gradual diminution in the

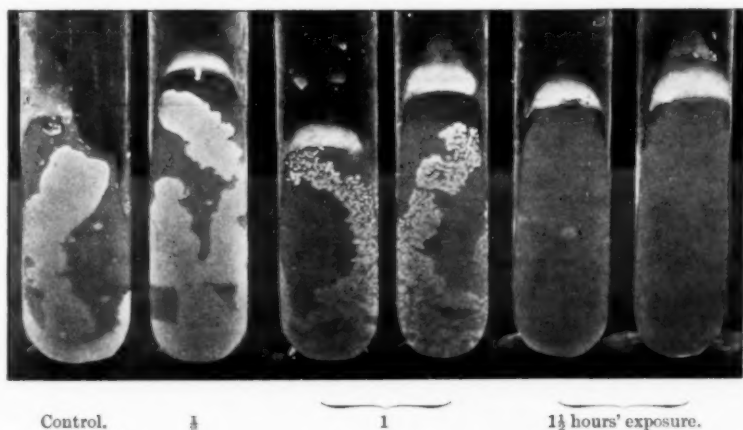


FIG. 2.

Action of radium emanation on *Bacillus coli communis*.

number of colonies for various times of exposure obtained in the manner indicated. Fig. 2 gives the result obtained with a concentration of 0.36 milli-curie per cubic centimetre, the emulsion containing 2.5×10^8 bacteria per cubic centimetre. Fig. 3 exhibits the contrast in effect obtained with the emanation and X-rays. The same emulsion was used

in the two cases, 0.67 milli-curie per cubic centimetre had a completely lethal action in four hours. Irradiation by soft X-rays for periods of three and six and a half hours had apparently a small inhibitory effect upon the number of colonies. Agglutination was observed after exposure to the emanation and the emulsion, originally neutral to litmus, gradually became acid. A series of observations with the clear fluid after centrifugalization of the emulsion similar to that detailed for *Staphylococcus pyogenes aureus*, showed that the *Bacillus coli communis* was appreciably affected by the acidity of the

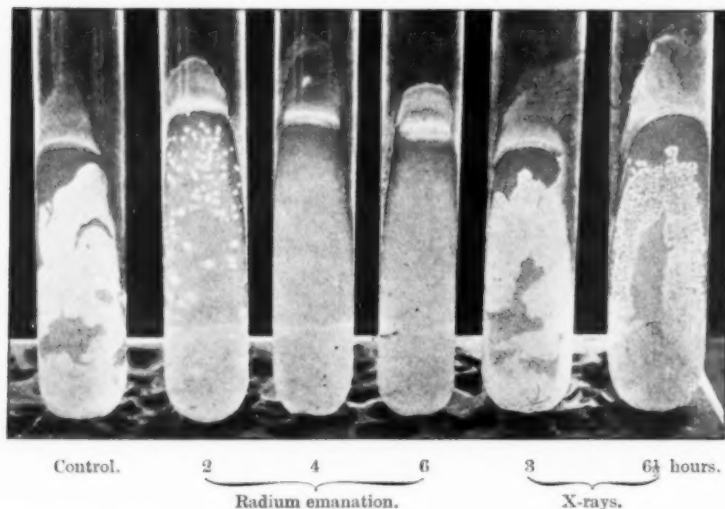


FIG. 3.

Action on *Bacillus coli communis*.

solution. A part of the original emulsion, after being mixed with an equal volume of the acid fluid and allowed to stand for twenty-four hours, showed a diminution in the number of colonies compared with the control, and this was more pronounced for longer intervals. The time taken, however, namely, several days, for a completely lethal action showed that the marked effects obtained with the emanation were not attributable to this indirect action.

Bacillus anthracis.—An emulsion in distilled water of anthrax bacilli from a twenty-four hours' agar culture was exposed to a concentration of 0.55 milli-curie per cubic centimetre. Equal volumes of the irradiated fluid were planted on agar after various times of exposure and incubated. From fig. 4 it will be seen that an almost complete lethal effect was obtained after three hours. Marked agglutination was observed after one hour's exposure. This is shown by the photomicrographs in fig. 5, which represent films of the control and irradiated emulsions one hour

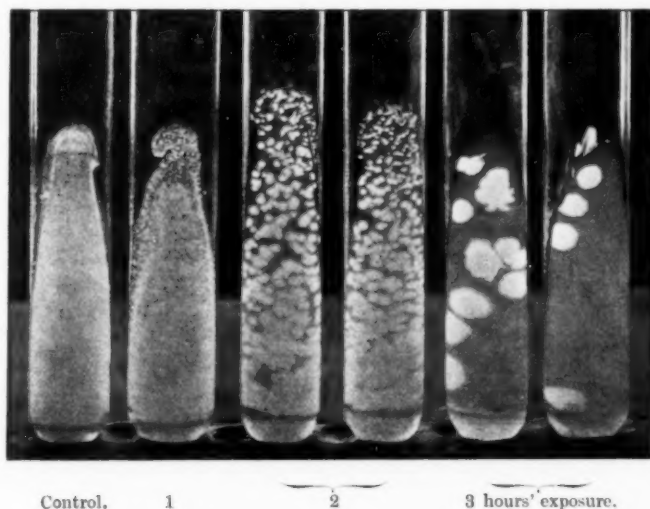


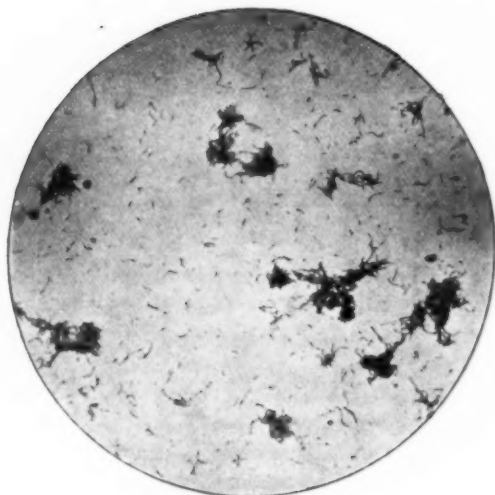
FIG. 4.

Action of radium emanation on anthrax bacilli.

after exposure had begun. After twenty-four hours' exposure the emulsion was centrifugalized and the effect of the supernatant fluid on an equal volume of the control emulsion tested. As in the case of *Staphylococcus pyogenes aureus*, the supernatant fluid had practically no lethal action upon the subsequent growth of the anthrax bacilli and did not cause agglutination.



Control.



Experimental.

FIG. 5.

Agglutination of *Bacillus anthracis* by radium emanation.

Anthrax Spores.—An emulsion of anthrax spores was found to be more resistant to the action of the emanation than the organisms hitherto dealt with. The result of exposing a thick emulsion, previously heated to 80° C. for half an hour, to 0.81 milli-curie per cubic centimetre may be seen from fig. 6. After an exposure of six hours to a more intense radiation than was used in any of the previous cases a small growth was still obtained. After more prolonged exposure, however, the spores failed

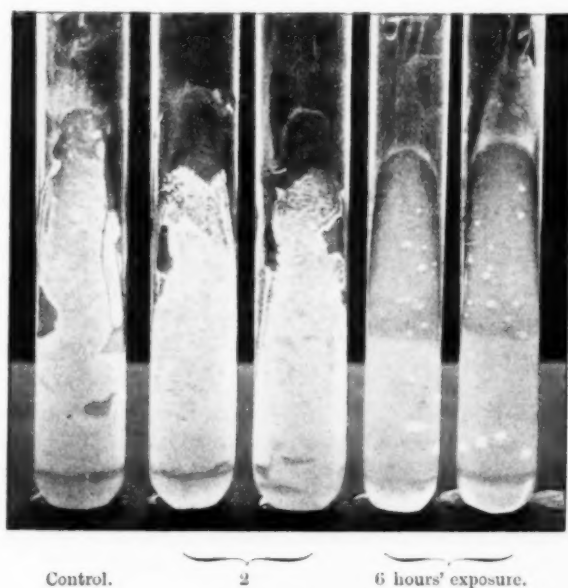


FIG. 6.

Action of radium emanation on anthrax spores.

to grow at all. Agglutination was observed after six hours and the fluid had become acid to litmus. The pathogenicity of the organism was shown by the subcutaneous inoculation of a mouse. The animal died in twenty hours and anthrax bacilli were cultivated from its blood.

THE EFFECT OF RADIUM EMANATION UPON MOTILE BACILLI.

The bactericidal action of the emanation upon *Bacillus pyocyaneus* is well marked, and its gradual destructive effect has been observed with the aid of the simple piece of apparatus of fig. 7, which allows of continuous observations being made upon the motile bacilli while under the influence of the emanation. It consists of a shallow brass box provided with side tubes for the in- and out-flow of the gas, and two glass windows in the base to allow of microscopic observations of hanging drops of the bacilli when placed over the apertures A and A¹. The hanging drops having been set up on slips of mica, the air is displaced by the emanation and continuous observations begin.

With a concentration of about 0.5 milli-curie per cubic centimetre in the box (volume about 5 c.c.) a diminution in motility is noted in

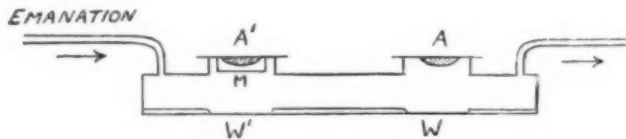


FIG. 7.

one hour; thence onward there is a tendency to agglutinate, and ultimately no motion is observed beyond Brownian movement. A platinum loop culture of the organisms at this stage fails to give any growth; in fact, before this stage is reached, when a movement of the bacilli is still visible, no growth is found to follow inoculation on agar. This is probably because the emanation goes into solution in the drop and its effects continue even after removal from the field of observation.

To show the special effectiveness of the emanation when dissolved in the bacterial emulsion, experiments were carried out in the following way. A film containing a hanging drop was placed over the aperture A, so that the emanation was free to go into solution in the drop; over the other aperture, A¹, was placed another hanging drop protected by a very thin sheet of mica which prevented the direct access of the emanation to the drop, but effected practically no absorption of the alpha and beta rays from the emanation within the box. The organisms in the uncovered drop quickly succumbed to the effect of the emanation,

whereas in the other they were still moderately motile after an exposure of several hours. As a typical example may be cited the exposure of two such drops to a concentration of 0.52 milli-curie per cubic centimetre. After three hours' exposure platinum loop cultures were made from the two drops. That from the uncovered drop remained sterile, whereas a moderate growth was obtained from the covered drop.

QUANTITATIVE DESTRUCTION OF THE ELEMENTS CONCERNED WITH PHAGOCYTOSIS.

The rays emitted by the emanation and its products are, generally speaking, destructive in their action. In view of some possible clinical applications of the bactericidal action of the emanation, it was desirable to make a quantitative estimation of its effects upon three of the constituents that enter into the process of phagocytosis—namely, bacteria, leucocytes, and the opsonin contained in normal serum. The result of this investigation is to show that the bacteria are much more affected by the emanation than the two other constituents.

(1) The procedure already described for measuring the bactericidal action was extended so as to obtain counts of the relative number of living bacteria in portions of the emulsion after various times of exposure. Measured volumes were diluted in sterile distilled water in steps of one hundred or less as required. Agar tubes were inoculated with equal volumes of these dilutions and plate cultures made. After incubation, counts were made of the relative number of colonies occurring in the various dilutions. The data contained in Table I refer to an emulsion of *Staphylococcus pyogenes aureus* in distilled water containing 3×10^9 organisms per cubic centimetre exposed to 0.48 milli-curie per cubic centimetre at about 4° C.

TABLE I.

Exposure to emanation, time in minutes		Number of colonies in 3×10^{-2} c.mm.		Logarithms of numbers
5	...	3,040	...	3.483
10	...	1,090	...	3.037
15	...	300	...	2.477
20	...	190	...	2.279
30	...	32	...	1.505
40	...	3	...	0.477

From the numbers in column 2 and the graph in fig. 8 it will be seen that after an exposure of half an hour to the emanation the

number of living bacteria is reduced to 1 per cent. of those initially present. If the logarithms of the numbers be plotted against time the points do not depart from a straight line more than can be attributed to experimental errors. This indicates that the destruction of the bacteria occurs at an approximately exponential rate.

TABLE II.

Exposure to emanation, time in minutes		Number of colonies in 10^{-2} c.mm.		Logarithms of numbers
5	...	6,200	...	3.792
10	...	4,450	...	3.648
15	...	1,800	...	3.255
20	...	445	...	2.648
30	...	162	...	2.210
40	...	60	...	1.778

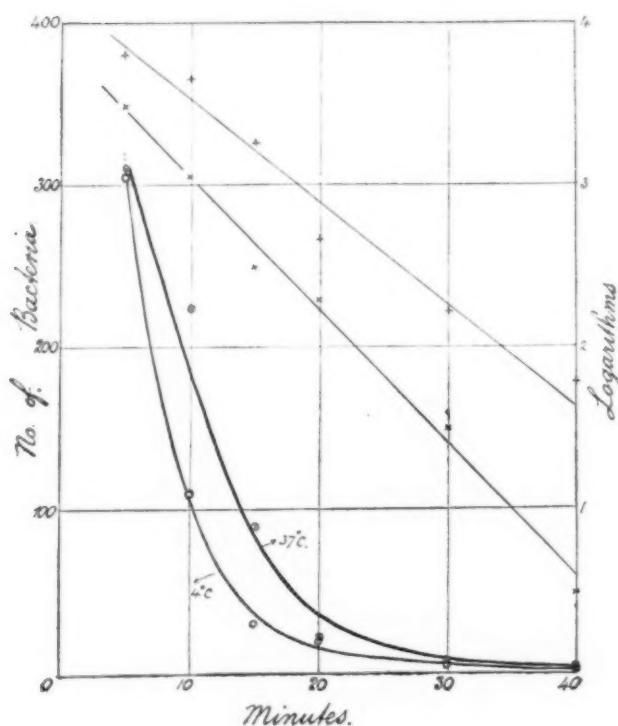


FIG. 8.

Under the conditions of this experiment, namely, at 4° C., the bacteria do not multiply. To see whether the bactericidal action of the emanation was in any way altered when the bacteria were placed under conditions favourable to their proliferation, an emulsion of *Staphylococcus pyogenes aureus* in broth at 37° containing 2×10^9 organisms per cubic centimetre was exposed to 0.2 milli-curie per cubic centimetre, and a series of observations made after various times of exposure in the manner detailed above. The number of colonies obtained from the same volume of irradiated fluid gradually diminished with time, as may be seen from the data in Table II and fig. 8.

By plotting the logarithms of the number of colonies against time, it was found that the destruction proceeds at an approximately exponential rate. From the slopes of the two logarithmic lines at 4° and 37° it was found that the rate of destruction was 1.32 times as great in the former as in the latter case, with, however, an intensity of emanation 2.4 times that which was experienced at 37° C. It seems, therefore, that the rate of destruction of bacteria by the emanation is not hindered under conditions favourable to their growth.

(2) The gradual diminution in phagocytic power of human leucocytes when exposed to the emanation was found by exposing them, after being washed in normal saline, to 1.6 milli-curies per cubic centimetre at 4° C., and after various periods of irradiation their phagocytic power was compared with that of a control portion of the same suspension of leucocytes. No degeneration was observed in the leucocytes during a period of eight hours' irradiation. Subsequently degenerative changes, vacuolation of the protoplasm, and defective staining of the nucleus, became increasingly evident, until eventually the leucocytes were destroyed. The procedure was that usually adopted for opsonic determinations, two volumes of the leucocyte emulsion being added to one volume of an emulsion of *Staphylococcus pyogenes aureus* and one volume of normal serum. The data contained in Table III and the graph in fig. 9 show the gradual reduction in phagocytic power of leucocytes when irradiated at 4° C.

(3) The quantitative reduction in opsonin, as evidenced by the usual opsonic estimations, under the action of the emanation was obtained by exposing normal serum to 1 milli-curie per cubic centimetre at 4° C. After various periods of irradiation the opsonic content of the serum was compared with that of the control portion by estimating the phagocytosis of an emulsion of washed leucocytes when mixed with an emulsion of

TABLE III.

Exposure to emanation, time in hours			Number of organisms in 200 leucocytes		Percentage of the control phagocytosis
Hours	minutes		Experimental	Control	
3	0	...	1,200	1,290	93
4	45	...	880	1,136	77
7	5	...	648	808*	61
				(corrected 1,060)	
8	0	...	468	1,008	46
9	50	...	464†	780	—

* The third control was subject to a technical error and is corrected to the value indicated by the remaining four observations.

† Numbers of degenerate leucocytes were observed, but not included in this count. Consequently the percentage of the control phagocytosis is not available.

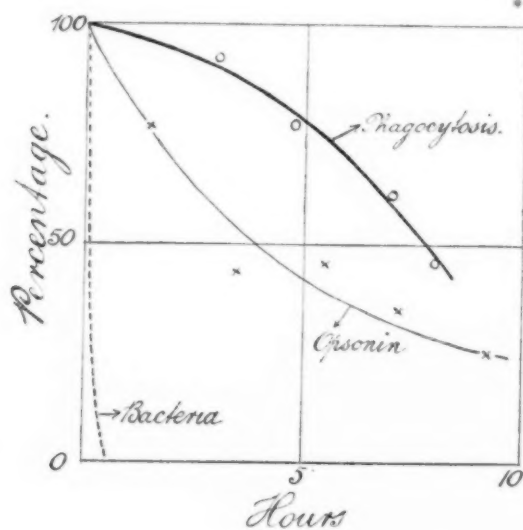


FIG. 9.

TABLE IV.

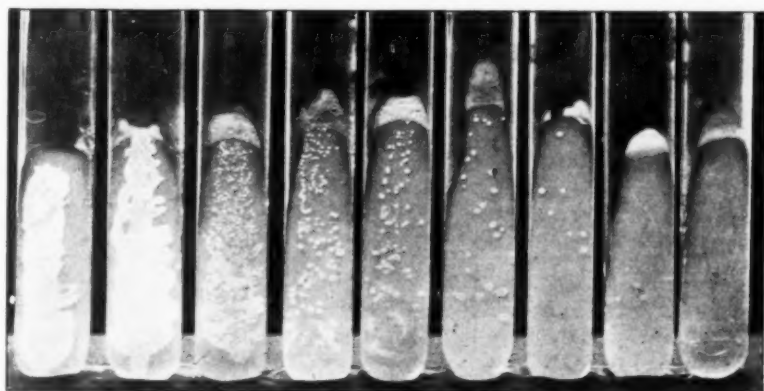
Exposure to emanation, time in hours			Number of organisms in 200 leucocytes		Percentage of opsonin
Hours	minutes		Experimental	Control	
1	30	...	520	622	77
3	30	...	267	605	44
5	30	...	275	596	46
7	15	...	223	636	35
9	15	...	143	558	26

Staphylococcus pyogenes aureus and either of the two sera. The gradual diminution in opsonin when the serum is irradiated is shown in Table IV and fig. 9.

Spontaneous phagocytosis was found to be 8 per cent. of the mean of the controls. It was thought unnecessary to correct the curve on this account. The behaviour of the three quantities under consideration upon exposure to the emanation is represented graphically in fig. 9. The intensity of the emanation in this series was 1.6, 1, and 0.48 millicuries per cubic centimetre for the leucocytes, opsonin and bacteria respectively. They are quantitatively affected in the inverse order: whereas the colonies grown from the bacteria were reduced to 1 per cent. of the number obtained from the control after an exposure of half an hour, the leucocytes when exposed to three times the intensity of emanation only suffered a reduction of 50 per cent. in their phagocytic power after about seven hours' irradiation, and the opsonin, on exposure to twice the intensity of emanation, was reduced to 50 per cent. in about four hours.

THE ACTION DUE TO THE ALPHA AND BETA RAYS.

Emulsions irradiated in the manner described are exposed to the alpha, beta and gamma rays from the emanation and its products. The



Control, 2 3 1/2 4 4 1/2 5 5 1/2 6 7 3/4 hours' exposure.

FIG. 10.

Action of beta rays on *Staphylococcus pyogenes aureus*.

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bactericidal effects which have been observed are due to the alpha and beta rays. Exposure of an emulsion of *Staphylococcus pyogenes aureus* to the gamma rays only, from 7 mgrm. of radium bromide, gave no evidence of any effect after an exposure of one week. When the beta rays from this source were utilized a completely lethal effect was obtained in six hours, as may be seen from the series (fig. 10).

CONCLUSIONS.

- (1) The emanation in concentrations of less than a milli-curie per cubic centimetre has a marked bactericidal action.
- (2) Agglutination of bacteria in distilled water is an early sequel to their irradiation.
- (3) Bacteria are more quickly destroyed by the emanation than are opsonin and leucocytes.

Pathological Section.

April 2, 1912.¹

On Certain Results of Drying Non-sporing Bacteria in a Charcoal Liquid Air Vacuum, &c.

By S. G. SHATTOCK and L. S. DUDGEON.²

De bacteriis in vacuo desiccandis.

SUMMARIUM.

MODUM quemdam in his experimentis adhibuimus a Dewar inventum, atque iis qui in rebus physicis versantur bene cognitum. [Explicationes vide figurarum.]

Lucis actio lethalis stricte excludebatur.

Ut observationes quam simplissimae fierent, illis solum bacteriis usi sumus quae nullos sporos generant.

Ex his observationibus invenimus Bacillum coli, bacillum quoque typhosum, in vacuo siccata, post paucos dies mori. Hi bacilli in aere suâ sponte desiccati, eodem temporis spatio moriuntur.

Staphylococcus pyogenes aureus, e contrario, vel in vacuo vel suâ sponte desiccatus, hebdomadas perstat plurimas antequam moritur.

Bacillus pyocyaneus facile resuscitari potest postquam in vacuo septem menses inclusus est.

In aere suâ sponte siccatus non perstat hic bacillus, mirabile dictu, nisi paucos dies.

Resistetne radiis solis Bacillus pyocyaneus in vacuo siccatus et dum in vacuo clausus, quum, tubis in aquâ submersis, absorbetur calor?

Experimento monstratur resistantiam non augeri.

¹ Laboratory Meeting, held at the Cancer Research Laboratories, Middlesex Hospital.

² This paper was communicated to the Royal Society by Sir James Dewar, February 10, 1912, but it has been in places modified for the present publication.

Hae observationes hypothesim ab Arrhenio nuper propositam vix confirmant: videlicet, bacteria in terram immigravisse de spatio extramundano lucis radiis propulsa.

Si ponitur, etenim, bacteria in vacuo extramundano vel desiccata vel gelata vagari, solis radiis cito destruerentur.

The following experiments were undertaken with the object of ascertaining whether non-sporing bacteria, dried *in vacuo* and kept *in vacuo*, would survive those dried in and kept in the air, or, on the contrary, whether they would die more rapidly. The action of sunlight and of heat was tested, moreover, upon bacteria dried *in vacuo* and kept *in vacuo*, with a view of discovering how far such agencies might be lethal upon dried bacteria, if the latter were supposed present in a free state in interplanetary space.

Effects of Drying.

In carrying out this work, we have had the invaluable advantage of Sir James Dewar's help, for of the several methods of drying *in vacuo*, by far the most efficient is that devised by him. This method is so well known to physicists that it will be enough to state here, that after the air of the vessel is exhausted by means of an air-pump, the glass connexion with the pump is sealed off in the blowpipe flame, and the exhausted chamber is deprived of its remaining gases through a second outlet communicating with a bulb containing cocoa-nut charcoal (previously freed from gases), which is submerged and kept in a Dewar vacuum flask of liquid air. The use of mercury was avoided in producing the initial vacuum, in order to exclude the presence of mercury vapour, which might in various ways invalidate the results of the experiments.

The apparatus was stored in a dark room to eliminate the action of light, and for the same purpose metal foil was wrapped around the tubes during the process of exhaustion with the pump. The charcoal at the temperature of liquid air has a remarkable capacity for gas absorption. The action of this substance was maintained sometimes for three days, sometimes for five, during which time the vapour of water distilled continuously, and was condensed on the walls of the condenser at -195° C. whilst the gases were absorbed by the charcoal. The way connecting the tube with the bulb of charcoal was then sealed off in the blowpipe flame, and the tubes were stored in light-tight photographic bags in a metal box, which was, furthermore, kept in a closed cupboard.

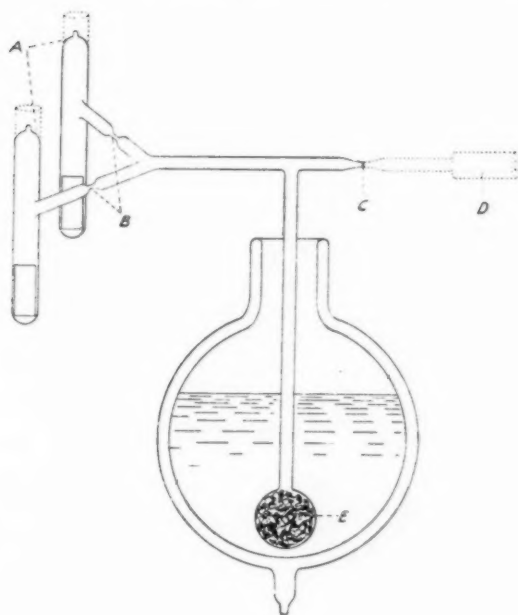


FIG. 1.

Explicatio figurae.

Monstratur apparatus ad bacteria in vacuo desiccanda aptus.

A, Tubi quorum extremitates superiores clauduntur postquam per eas introductae sunt laminae vitreae bacteriis oblitae.

B, Tubuli laterales qui clauduntur postquam vacuum perfectum est carbonis auxilio in bulbo inclusi, bulbo ipso in aere liquido nunc tres, nunc quinque dies submerso.

C, Tubus qui clauditur postquam aer antliæ exhaustus est.

D, Tubus quo apparatus cum antliâ jungitur.

E, Bulbus in quo carbo continetur, in aere liquido submersus.

The arrangement adopted for the purpose of drying the slips of glass smeared with the bacteria.

A, Open test-tubes sealed at the upper ends after the inoculated glass slips have been introduced.

B, Side tubes sealed off after the completion of the vacuum by means of the charcoal and liquid air.

C, Tube sealed off after the air has been as fully as possible removed by the exhaust pump.

D, Connexion to the rotatory exhaust pump.

E, Bulb containing 5 grm. of cocoa-nut charcoal, submerged in a Dewar vacuum flask of liquid air, in order to complete the vacuum after the action of the exhaust pump.

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The possible ways in which the vacuum may suffer are (1) in sealing off the side outlet, by the evolution of gas from the heated glass; (2) owing to the presence of microscopic fissures at the junctions of the apparatus, especially if many chambers are connected up with the same charcoal receptacle; (3) by reason of the fact that glass is hygroscopic, and that even after a prolonged period of high exhaustion, water might fail to be removed, at the ordinary temperature, from the inner surface of the vacuum tube or from the glass slip inoculated with the organic film of peptone containing the micro-organism.

The vacuum tubes employed were stout test-tubes of soft glass, furnished with a side channel by means of which they were connected (1) with the exhaust pump, and (2) with the bulb of charcoal. (See figures.)

The inoculations were made upon rectangular slips of thin glass (No. 2 microscopic cover) by means of a large platinum loop, the slips having been previously heated for one hour at 150° C., in the Petri dish in which they were afterwards inoculated. The immediate drying of the slips after the inoculation was carried out in the incubator at 37° C., in which they were kept for about fifteen minutes.

Some of the slips were, within the course of an hour or so, transferred to the tubes, from which the air was thereupon exhausted; the rest were stored in the Petri dish in the dark. The bacterial suspensions first used were made by adding boiled water to a recent agar or jelly slope culture; all the later suspensions were cultures in peptone water (with 1 per cent. sodium chloride).

In order to test the vitality of the bacilli after drying, whether *in vacuo* or in the air in the Petri dish, the slips were transferred to test-tubes of litmus glucose broth, and incubated for many days at 37° C. The broth tubes were proved to be sterile before use, by a preliminary incubation.

We may now proceed to detail the observations, and afterwards to comment on the results.

Bacillus coli.

The first experiments were made upon this bacillus on October 14, 1910.

One vacuum tube was sealed off after three full days' connexion with the charcoal tube—i.e., on the fourth day, and a second on the sixth day, the vitality of the micro-organism being tested as above described. In both cases it was dead. The control air-dried film was also found to be dead on the fourth day.

Bacillus typhosus.

Vacuum tubes were sealed off on the fourth day and on the sixth.

The bacillus in both proved to be dead. The control air-dried films were likewise dead on the fourth day. The exact day on which the air-dried micro-organism dies can be, of course, readily determined by transferring an inoculated slip daily to the broth medium.

Different strains or samples of the same bacillus vary within certain limits. In an observation so made, using for the inoculation a suspension

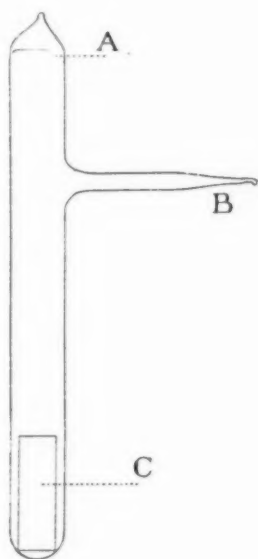


FIG. 2.

Explicatio figurae.

A, Extremitas tubi superior quae clauditur postquam introducta est lamina vitrea bacteriis oblita.

B, Tubulus lateralis cum antliâ bulbo quoque carbonem includenti communicans. Hic tubulus postquam vacuum perfectum est clauditur.

C, Lamina vitrea bacteriis oblita.

A, Open end of test-tube, sealed off after the introduction of the inoculated slip of glass.

B, Side tube connected with the exhaust pump and also with the glass bulb containing the cocoa-nut charcoal. This is sealed off in the blowpipe flame after the full completion of the vacuum.

C, Slip of thin glass on which is the dried bacterial film.

of *Bacillus typhosus* in water from an agar slant of twenty-four hours' growth, the bacillus died on the fourth day. In four experiments made with a twenty-four hours' growth in peptone water of *Bacillus typhosus*, the micro-organism died, in one case on the first day (i.e., within twenty-four hours), in two cases on the fourth day, and in the fourth case on the fifth day.

Staphylococcus pyogenes aureus.

This is more resistant to desiccation, both *in vacuo* and in the air, than either of the preceding. In one experiment vacuum tubes were sealed off on the fourth day and on the sixth. The staphylococcus grew abundantly in both cases within twenty-four hours. The control air-dried slips prepared at the same time grew equally rapidly after the same periods; further controls proved to be alive on the sixteenth and twenty-third days, but when again tested on the fortieth day the microbe was dead.

By means of a second series of observations the survival of the staphylococcus *in vacuo* on the fourth and sixth days was confirmed, the control slips in this case being likewise alive on the same days.

As it was thus clear that the staphylococcus would survive drying five days *in vacuo*, and also in the air, we proceeded to test its vitality for longer periods. Vacuum tubes were sealed off after five days' treatment with the charcoal and liquid air, and stored in the dark. The micro-organism from the tubes proved to be alive on the thirty-third day, and so was the control. Further control slips were tested at different periods, and proved to be alive at nine weeks four days; death had occurred at twelve weeks four days, the microbe having died at some date in the interval.

As the control was now dead, a vacuum tube was tested twenty-one days later; the film proved to be sterile. In this experiment the air-dried slips died at some date between nine and twelve weeks; those from the vacuum tubes died between four and fifteen weeks.

(Two further vacuum tubes were tested at periods of ten and fourteen months; the slips from both were sterile.)¹

¹ Paul and Prall have studied the value of disinfectants upon staphylococci dried on the surface of garnets at the temperature of liquid air, by which latter treatment they also found that the micro-organism was not killed. "Die Wertbestimmung von Desinfektionsmitteln mit Staphylokokken die bei der Temperatur der flüssigen Luft aufbewahrt wurden," *Arch. d. d. Kaiserl. Gesundheit.*, Berlin, 1907, xxvi, pp. 73-129.

Bacillus pyocyaneus.

The results obtained with this bacillus are particularly interesting.

Films of the micro-organism, prepared as usual from a twenty-four hours' peptone water culture, proved to be alive on the fourth and sixth day when removed from vacuum tubes treated for these periods with charcoal and liquid air. Control air-dried slips were likewise alive at the same dates. The vitality was next tested for longer periods.

December 9, 1910: A series of glass slips were inoculated. One slip was transferred to each of three tubes, which were thereupon exhausted, and sealed off after five days' treatment with charcoal and liquid air.

A control slip proved to be alive on the sixth day. One vacuum tube was opened on the forty-sixth day—the bacillus proved to be alive; a control film was at this date dead.

A second vacuum tube was opened on the one hundred and sixteenth day; the bacillus was still alive. The third of the tubes was opened on June 30 (seven months and seven days); within forty-eight hours an abundant growth of the bacillus (as confirmed by sub-culture) had occurred.

In confirmation of this remarkable longevity *in vacuo*, in a second set of observations, *Bacillus pyocyaneus* was found to have remained alive from May 26, 1911, to December 16, 1911—a period of exactly the same length as the above.

One slip was tested on June 1, 1911, and was found alive. The growth obtained from the slip on December 16 was in every way characteristic. Within forty-eight hours the litmus glucose broth was uniformly turbid, and was decolorized except for a zone at the free surface, which retained a violet tint; the top of the fluid was covered with a thin, unwrinkled, faintly greenish looking scum or zoogloea. Sub-cultures carried to peptone water on December 18 showed within twenty-four hours general turbidity, and a delicate but well-marked green coloration; a sub-culture from this carried to an agar slant gave within twenty-four hours a full growth, which within forty-eight hours had produced a typical green pigmentation of the medium in the neighbourhood of the culture.

The longevity of this bacillus *in vacuo* is the more remarkable since the micro-organism somewhat rapidly dies in air-dried films. Under the latter circumstances the date of death (as tested by daily transferring a slip to a broth tube) varies within certain limits; but we have never found the microbe alive after the ninth day.

Remarks.

Taking the results obtained by complete drying *in vacuo*, two obvious conclusions will appear. In the first place it is clear that the vulnerability of different bacteria varies within wide limits. And in the second, as the vitality of *Bacillus pyocyaneus* *in vacuo* is notably prolonged beyond that of air-dried slips, the prolongation can only be due to the absence of chemical changes which obtain in the air, but are absent in the vacuum.

In regard to the first of these two results we may provisionally hold that it implies a difference in the composition or the molecular construction of the protoplasm. It has a parallel in the difference of resistance to heat. The thermophilic bacteria thrive at a temperature of 70° C., whilst the common death-point of other (non-sporing) forms, when suspended in fluid, ranges close about 60° C.

The different resistance of different bacteria to drying *in vacuo*, and to heat, indicates that the chemical constitution, or the molecular construction, of the protoplasm varies; that protoplasm is not a definite chemical substance, but one of varying range.

The selection of particular body-cells by particular poisons is one proof of such a difference in the same organism. It is probably correct, indeed, to hold that every functional difference amongst cells implies a protoplasmic one. *Quot actiones tot protoplasmata*. And the same of bacteria, physiologically considered. How long *Bacillus pyocyaneus* will live in the dried state *in vacuo* is an interesting question, and we have a series of vacuum tubes sealed off to keep (excluded from the light) for protracted periods, with a view of testing it.

In the air-dried state *Bacillus pyocyaneus* presents no particular longevity. Its death under these circumstances cannot be ascribed simply to its drying. The film may absorb moisture at intervals according to the saturation of the atmosphere, and the bacillus may be killed by a recurrent process of oxidation. Or dissociation may occur in some of the less stable constituents of the protoplasm. In the vacuum tube oxidation would be excluded, but dissociation or autolysis might occur, and eventually prove fatal.

In the case of *Staphylococcus pyogenes aureus*, which survives some weeks *in vacuo* and then dies, something of the latter kind may be assumed, by way of exclusion, to take place.

Yet whether protoplasmic autolysis could occur in the absence of moisture is a matter open to grave doubt, for it is at the present time an

established fact that very few examples can be adduced in which chemical processes take place without the presence of water; even the combination of oxygen and hydrogen fails, at the melting point of silver, if both gases are absolutely dry. It must be borne in mind in this connexion that by the method of drying adopted, all the water associated with the bacillary protoplasm is removed. That water is held in different degrees of closeness even in inorganic compounds, appears from the well-known fact with regard to copper sulphate. Each molecule of this salt holds five of water in association. Of these, four can be disengaged at 100° C., but the fifth requires a temperature of from 210° to 240° C. Notwithstanding, the charcoal liquid air vacuum will remove the whole of this water (Sir James Dewar): and so with respect to the residuum of water left in association with the protoplasm after ordinary drying, and which is removed at 110° C.; the whole is extracted by the method adopted, and the desiccated substance reabsorbs water on being introduced into the culture broth, and reverts to its original state of hydration.

It may be pointed out that these differences in resistance to drying *in vacuo* cannot be ascribed to the chemical differences indicated by Gram's staining reaction. *Staphylococcus pyogenes aureus* (Gram-positive) is, it is true, more resistant than *Bacillus coli* or *Bacillus typhosus* (both Gram-negative), but the most resistant of all, *Bacillus pyocyaneus*, is, like the last, Gram-negative.

The ordinary microscopic examination does not reveal any recognizable change in bacilli which have been long dried. A dried peptone water film of *Bacillus pyocyaneus*, made on November 26, 1910, and stored in the dark, in a Petri dish, showed, when stained with carbol fuchsin, and examined with $\frac{1}{12}$ immersion, on June 15, 1911, nothing in which it would differ from a recently made preparation. And the same is true of *Staphylococcus pyogenes aureus*.

A similar film of *Bacillus pyocyaneus* made in July, 1911, was examined in January, 1912, in a hanging drop, which was prepared by wetting the dry film with germ-free distilled water, and transferring a loop of the suspension to a cover-glass. The bacilli after imbibition of water were of full size, and perfectly normal in form.

The results of drying in the case of the seeds of phanerogams have often been made the subject of observation, but it is only recently that scientifically conducted experiments have been carried out in this connexion—by Becquerel, who has adopted the method of drying

seeds for prolonged periods *in vacuo*. The inquiry is here complicated by the protection afforded by the testa or covering with which such seeds are provided. This is one reason, we venture to think, why our experiments made upon non-sporing bacteria are of greater value from the biological standpoint; they are clearer and more decisive in result, and show unequivocally that the protoplasm when completely deprived of water may still retain its vitality. The older observations upon the resistance of seeds to drying are defective for the reason that they do not determine whether the cell-protoplasm of the embryo has been dried, or whether the cells have retained water owing to the impermeability of the testa. That seeds will germinate after having been dried for prolonged periods in the air has been long known. In the *Philosophical Transactions of the Royal Society* (vol. xlii, 1742, p. 115) there is a note by Martin Triewald, F.R.S., to the effect that he sowed two dozen melon seeds, which had been wrapped up in paper in the year 1700: of these, twenty-one furnished good plants. Gérardin¹ found that haricot seeds taken from Tournefort's herbarium, and which were over one hundred years old, would germinate. But the longest authenticated record is that established by Robert Brown. In 1827 this celebrated botanist was appointed keeper of the Botanical Collection at the British Museum, which comprised the herbaria of Sir Joseph Banks, and of Sir Hans Sloane (1660-1753). He is stated, in 1850, to have sown samples of certain of the seeds contained in the Sloane Collection. These would be about one hundred and fifty years old; yet many of them germinated.² In regard to longer periods than this no similar direct proof is at present forthcoming; as, for example, in the case in which Professor Heldreich, of Athens, found about the mines of Laurium in 1873 a new species of *Glaucium*, which had appeared on land from which there had lately been taken a thick layer of scoria coming from the ancient exploitation of mines, at least fifteen hundred years ago: the suggestion here made is that the seeds had persisted in a living condition for this prolonged period. The alleged germination of the Egyptian mummy wheat which was placed in the tombs along with date fruit, grapes, bread, &c., for the sustenance of the departed spirit,

¹ Alph. de Candolle, "Introduction à l'étude de la botanique," 1835, i, p. 375.

² Cited by C. de Candolle, "Sur la vie latente des graines," *Arch. des Sci. phys. et naturelles*, xxxiii, Juin, 1895. We have been unable to discover a reference to this experiment in the collected publications of Robert Brown, in the library of the Linnean Society.

is universally held at the present time to have rested upon error, which appears to have arisen from the fact that mummies intended for exportation to Europe have at times been packed in recent grain, and that this has erroneously been assumed to be ancient. In every instance in which mummy wheat of known ancient source was experimented with at Kew Gardens, the grain proved to be dead.

The problem, as already stated, is here complicated by the fact that the seed covering, in the case of certain natural Orders, notably the Leguminosæ, is impermeable, and that complete drying of the contents is thus effectively prevented for prolonged periods.

Becquerel¹ has shown that the dry testa of a pea or bean is quite air-tight, as tested by fitting detached pieces so as to close the top of the tube of a Torricellian vacuum; even the micropyle is hermetically sealed in a way which allows no air to pass. In order to dry such seeds the testa must be perforated; they are then kept (by Becquerel's method) for three months *in vacuo* at 45° C., in the presence of caustic baryta; seeds which have been perforated, fully dried, and kept for two years in a high vacuum, exhibit no loss of germinating power. The results accord with those obtained by ourselves upon *Bacillus pyocyaneus* except that they are less unequivocal by reason of the bulk of the material to be dried, and the difficulty presented, even after perforation of the testa, to the ready passage of water through the dried cellulose walls of the component cells.

The Persistence of Vitality in Bacteria in the Dried State *in vacuo*, and the Question of their Resistance in this Condition to Physical Agencies.

The most fascinating problem in connexion with the vitality of bacteria *in vacuo* is the possibility of their interplanetary life.

That certain bacteria can survive in a fully dried state *in vacuo* is as important a fact in this connexion as that so many may be frozen at the temperature of liquid air (−195° C.) without being killed.

Particulate life, whether microscopic or ultra-microscopic, if free under interstellar conditions would exist *in vacuo*; and, either in a dried state, or impregnated with water, it would be cooled to a temperature certainly as low as that of liquid air.

¹ *Ann. des Sci. Nat. (Bot. Ser. IX)*, 1907, v, pp. 193-310.

The external agencies adverse to life in such circumstances resolve themselves into the action of the solar rays: heat, light, ultra-violet, and the corpuscular radiations.

HEAT.

If the inoculated slips of *Bacillus pyocyaneus* in sealed vacuum tubes be submitted to the action of heat, the vulnerability of the bacillus to this agency is not found to be lessened. It has long since been established that many bacteria, even of the non-sporing kinds, withstand a higher temperature in the dry state than in the wet. Suspended in a fluid medium, *Bacillus pyocyaneus* is killed by a temperature of 60° C. after an hour's exposure.

In testing the effect of heat upon this bacillus in the dried state, we commenced with a temperature which is lethal to all non-sporing pathogenic bacteria, in order to ascertain whether its resistance *in vacuo*, if exalted, was exalted in a pronounced degree.

July 20, 1911: A vacuum tube containing an inoculated slip of *Bacillus pyocyaneus*, which had been sealed off on July 17 and kept in the dark, was baked in the hot-air oven for three hours, between 102° and 104° C.

No growth occurred from the slip when transferred to litmus glucose broth and incubated at 37° C.

A control slip, prepared on July 20, and baked simultaneously for the same time in a test-tube, over which a second larger tube was inverted, for protection, likewise proved to be sterile.

In the following experiment, the air-dried films of *Bacillus pyocyaneus* were subjected to a temperature of 100° C. in a water-bath, for considerably shorter periods.

January 6, 1912: A series of slips were prepared from a twenty-four hours old peptone water culture of *Bacillus pyocyaneus* in the usual manner. Three were then transferred, each to a long sterilized test-tube of thick glass; the tubes were thereupon sealed in the blow-pipe flame by heating each at a considerable distance below the open end. The three tubes were, in the next place, submerged by means of strips of lead in a vessel of warm water and boiled for fifteen, thirty, and sixty minutes. One end of the tube was cut off with a file, and the slip transferred to a tube of litmus glucose broth, and incubated at 37° C.

After this, a control slip from the Petri dish was placed into another tube of the same medium and incubated with the rest. No growth ensued in the case of any of the three heated slips; the control gave a full growth of *Bacillus pyocyaneus* within forty-eight hours.

January 13, 1912: It being thus clear that the air-dried film of *Bacillus pyocyaneus* is killed by fifteen minutes' heating at 100° C., a vacuum tube containing a slip of this bacillus, which had been sealed off August 1, 1911, after the usual treatment, was boiled for forty-five minutes.

The time selected was triple that of the minimum which had been found lethal in the case of the air-dried film. The purpose of this was to ensure that the film was raised to the temperature of 100° C., seeing that its heating *in vacuo* would be delayed, owing the absence of gas convection, and could occur only by radiation, and conduction from the heated tube to the edges of the glass slip in contact with its inner surface. After being boiled for forty-five minutes, the tube was opened with the usual precautions, and the slip transferred to litmus glucose broth, and incubated at 37° C.

A second vacuum tube was then opened as a control, and the contained slip transferred to another tube of the same medium; the vacuum tube was one of four which had been sealed off at the same time, viz., August 1, 1911; the slips in these four tubes have been inoculated from the same peptone water culture of *Bacillus pyocyaneus*. The slip from the boiled tube proved to be sterile; that from the control tube gave an abundant growth within forty-eight hours, which was identified by sub-culture as *Bacillus pyocyaneus*.

Proceeding with temperatures lower than 100° C., air-dried slips of *Bacillus pyocyaneus* (prepared as in all other cases, for the immediate occasion) were treated in sealed tubes by submersion in water at 80° C., after having been warmed for fifteen minutes at the innocuous temperature of 40° C. One slip was heated for thirty minutes, one for sixty. Both proved to be sterile. The air-dried, unheated, control slip, which was transferred to broth after the completion of the heating of the others, gave a full growth.

By the same method it was found that temperatures of 76° C. and of 65° C. are lethal when maintained for an hour.

The results show that in the case of *Bacillus pyocyaneus* the lethal temperature is practically the same, whether the micro-organism is subjected to it in the wet state or the dry.

We terminated these observations by heating a vacuum tube containing a slip of *Bacillus pyocyaneus*, sealed off August 1, 1911, for three hours at 65° C. in a water-bath. The film proved to be dead. The control, unheated, film in another vacuum tube of the same batch (August 1, 1911), tested on the same day, gave a typical and abundant growth within forty-eight hours.

It appears plainly, therefore, from these observations that the resistance of *Bacillus pyocyaneus* to the action of heat is not heightened when the micro-organism is exposed to this agency in the dried state *in vacuo*.

SUNLIGHT AND ULTRA-VIOLET RAYS.

The lethal agent of first importance, however, in connection with supposititious interplanetary life in a free or unincluded condition, is sunlight. As this reaches the deeper strata of the atmosphere, the ultra-violet rays are filtered out of it. Notwithstanding this, its lethal properties in regard to bacteria have been long established; even endospores are killed by it.

Is the dried *Bacillus pyocyaneus* killed, *in vacuo*, by the action of sunlight? This question must be answered in the affirmative.

In the following observations the action of the sun's heat was eliminated by submerging the tubes in a large shallow glass dish of water, by means of strips of lead wrapped round their ends. The glass dish was raised some way from the ground by allowing its two ends to rest upon the edges of two stools. The apparatus was exposed on a roof during the unusually bright weather of July and August, 1911. The inoculated glass slip was displaced by tilting the tube, to the centre of the latter, and in such a way that the flat surface lay upwards.

July 22, 1911: A vacuum tube containing a slip of *Bacillus pyocyaneus*, which had been sealed off on July 17, 1911, after three days' treatment of the vacuum by means of charcoal and liquid air, was exposed, as described, from 11.15 a.m. for six hours, the sunlight being intense and not at any time interrupted. The tube was then opened, and the slip transferred to a tube of litmus dextrose broth. No growth ensued.

July 20: A second vacuum tube, sealed off on July 17, was exposed, as detailed, from 1 p.m. for four hours. For portions of the time the sun was behind clouds.

July 21 : The tube was a second time exposed (after being stored in the dark) from 11 a.m. for six hours, the sunlight being on this occasion intense and uninterrupted. The slip was then removed and transferred to litmus glucose broth. No growth ensued.

A control tube made by inserting an air-dried slip prepared from a peptone water culture on the morning of the experiment, July 20, into a test-tube of stout glass and sealing the end in the blowpipe flame, was exposed for the same two occasions in the same dish of water: the slip, on being transferred to a tube of the same medium, viz., litmus glucose broth, proved sterile.

Another control tube was exposed on July 20 for four hours (sunshine interrupted), and the slip of *Bacillus pyocyaneus* then transferred to a tube of litmus glucose broth; it gave a characteristic growth.

As a comparable test of the action of sunlight upon *Bacillus pyocyaneus* in the moist state, an agar slant from which the water of expression had gone, was inoculated, without disturbing the surface, with a twenty-four hours' growth of the bacillus in peptone water. The end of the tube was sealed in the blowpipe flame, and the tube was exposed on July 20, in the same dish of water as used on that day for certain of the observations already recorded, for four hours' sunshine (interrupted). The end of the tube was then removed, and the agar medium covered by pouring in litmus glucose broth; the tube was thereupon plugged with sterilized wool.

A growth of the bacillus (identified by sub-culture) followed in this case as in that of the dried film exposed for the same time on the same day.

A second control made in precisely the same way upon an agar slant, from a twenty-four hours' growth in peptone water, and exposed on July 21 for five and a half hours' uninterrupted sunshine (from 11.30 a.m. to 5 p.m.), proved sterile, like the dried slip from the vacuum tube exposed to uninterrupted sunlight for six hours.

It is thus abundantly clear that bright sunlight is lethal within six hours to *Bacillus pyocyaneus* in the dried state, *in vacuo*, and that the resistance of the dried bacillus to this agency is not materially exalted, if it is increased at all, under the condition last stated.

The results show, in passing, that the view sometimes taken of the lethal effect of sunlight upon bacterial cultures, viz., that it is due to chemical decomposition of the medium on or in which the micro-organism is growing, is unnecessary to explain the result; and they equally disprove the view adopted by Roux, that the effect is brought

about by oxidation occurring through the intermediation of the air surrounding the organism.

This being so, it was, perhaps, hardly necessary to test the lethal action of the short wave-lengthed ultra-violet rays upon the dried bacillus, except for the sake of confirming an obvious deduction by actual demonstration.

In the following experiment, the action of the ultra-violet rays was tested upon *Bacillus pyocyaneus*, which had been dried *in vacuo*, but upon the slip after its removal from the vacuum tube, and in an atmosphere of nitrogen.

It may be noted here that the intense light generated by the apparatus is *per se* also lethal, but not within the same time. This admits of being demonstrated by intercepting the passage of the ultra-violet rays by means of mica.

May 26, 1911: A set of slips was inoculated with a twenty-four hours' growth of *Bacillus pyocyaneus* in peptone water. A slip was transferred to each of four tubes, which were then exhausted, &c., and kept for five days, connected with the bulb of charcoal surrounded with liquid air.

May 31: One of the tubes was opened, and the slip removed and exposed in an atmosphere of nitrogen for fifteen minutes to the action of the ultra-violet rays. The slip was then transferred to a tube of litmus dextrose broth, and incubated at 37° C. as usual. The object of carrying out the exposure in nitrogen is to prevent the formation of ozone from the atmospheric oxygen, which would *per se* be lethal.

A second vacuum tube was then opened, the slip removed, and exposed in the same way to the rays for thirty minutes, after which it was transferred to a tube of litmus dextrose broth. No growth occurred in either tube, proving that the action of the ultra-violet rays in an atmosphere of nitrogen had been lethal.

June 1: Another of the same batch of vacuum tubes was opened, and the slip transferred to litmus dextrose broth. A growth of *Bacillus pyocyaneus* had occurred within twenty-four hours.

The details of the technique employed, which were devised by Sir James Dewar, were as follows: The air admitted to the vacuum tube, after being sealed off, was air which had been dried and deprived of particulate material, by passing it through a U-tube containing cotton-wool, immersed in liquid air.

The slip was transferred, with the film uppermost, to a capsule of German silver, into which, near the bottom, a side tube was soldered, this being connected with leaden tubing to a Dewar vessel containing liquid nitrogen, from which the gas was regularly discharged by slow ebullition throughout the experiment.

The German silver capsule was fitted with a lid of quartz, and placed in a beaker of pounded ice. The lid of quartz was made to fit fairly tightly inside the upper part of the metal capsule, so that the nitrogen could only slowly escape from the chamber.

After two or three minutes to allow of the replacement of the air by the nitrogen, the ultra-violet rays were switched on. The distance from the horizontal quartz tube, whence the rays were emitted from the arc passing between two mercury poles, to the top of the capsule was about 2 in.

May 26 : This observation was repeated in all details, upon slips of *Staphylococcus pyogenes aureus*, which had been dried *in vacuo* for the five preceding days, the connexion with the bulb of charcoal, &c., being maintained throughout. Four tubes were sealed off, and on the same day two were opened, the slips removed, and subjected, with the prepared side upwards, to the rays, for fifteen and thirty minutes respectively. After the exposure, each slip was transferred to a tube of litmus dextrose broth. No growth took place in either tube.

June 1 : A control vacuum tube sealed off on May 26, after five days' connexion with the bulb of charcoal and liquid air, was opened, and the slip transferred to a tube of litmus dextrose broth. Growth occurred within twenty-four hours.

The Problem of Interplanetary Life.

We may conclude with a brief statement of the views which have been advanced upon this subject, since the experiments detailed in the foregoing communication have a distinct bearing on the theory recently developed by Arrhenius¹ as an alternative to that first proposed by Lord Kelvin. Lord Kelvin's suggestion was made in his Presidential Address to the British Association meeting held in Edinburgh in 1871. It supposed, what is known to astronomers to be of undoubted occurrence, the collision of two great masses in space: the heat so generated would reduce a large part of the colliding bodies to a molten or gaseous condition, but a quantity of débris, it is assumed, would be shot forth in all

¹ Svante Arrhenius : " Worlds in the Making," Stockholm ; English Trans., 1908.

directions; and the author conceived of huge fragments so detached, as carrying living plants and even animals, which fragments might, as meteorites, fertilize any planet on which they chanced to alight, should the other necessary conditions obtain. The criticisms of Arrhenius (*loc. cit.*) to this suggestion are: That it is questionable whether anything living would survive such a collision of two worlds: meteorites become incandescent on the surface during their fall; they are different in composition from fragments of the surface of the Earth or similar planet; plants develop almost entirely in loose soil, and a mass of such, falling through our atmosphere, would be disintegrated into a shower of small particles by the resistance of the air; each of these particles would flash up like a shooting star, and would not reach the surface in any other form than that of burnt dust.

Some of these objections may be met without much difficulty. The living forms on such fragments might be bacteria sequestered in deep fissures; and as the incandescence of a meteorite of magnitude, on traversing the earth's atmosphere is confined to the exterior, the heat transmitted within, were the material a bad conductor, would not of necessity kill the included micro-organisms. On such a protoplasm-bearing meteorite being fractured or disintegrated after fall, the dormant organisms included within it would find their opportunity for resuscitation and propagation, did they meet with a suitable pabulum and the right environment: the mass might even fall into a lake—that would give a still better chance to the contained bacteria.

There is, moreover, a second conceivable mode in which meteorites might arise, viz., by the internal, explosive, disruption of a single sphere; and in this case, there being no impact in question, the temperature of the surface-fragments would not necessarily be raised to any very high degree. It will be obvious, nevertheless, that such a supposition as Lord Kelvin's only shifts the origin of particulate life a step further back: the source of life upon the world from which the meteorite was detached would present the same original problem for solution.

The hypothesis of Arrhenius is an application of the established physical fact that waves of light and of heat exert a measurable pressure upon the body on which they fall; and that if the material is sufficiently finely divided, it will be propelled away from the source of energy. The general term "radiation pressure" is that adopted by Arrhenius to include the whole of such phenomena. This pressure in intermundane space is calculated to be four times as great as that of gravitation.

The second and *unproven* part of the Arrhenian theory is the doctrine of Panspermia which accompanies it—viz., that interplanetary space is pervaded with living microscopic and ultramicroscopic germs which are amenable to such propulsion. Assuming, however, this to be the case, the radiation pressure of the sun would in the course of time propel such germs from the intermundane vacuum into the rarer periphery of the earth's atmosphere whence they would eventually be conveyed by other agencies to the surface: and here they would germinate on meeting with the necessary conditions. The theory would imply not only that this has at some remote date happened, but that it is still taking place; though its author admits the practical impossibility of identifying any new micro-organisms which might in this way find a habitat on our planet. The cold in the intervening vacuum, calculated to be about -220° C., would suspend the life of such germs without destroying them. This last deduction is founded upon the well-known experiments carried out by Allan Macfadyen¹ in conjunction with Sir James Dewar twelve years ago.

Various bacteria, amongst which were included *Bacillus typhosus* and *Bacillus anthracis* (sporing culture), were hermetically sealed in fine glass tubes, and kept submerged in liquid air for seven days, without their vitality being impaired. In a further experiment, the tubes were submerged for ten hours in liquid hydrogen (-252° C.), with the same negative result. Brown and Escomb had previously shown that the seeds of phanerogams were uninjured by submersion in liquid air.² This observation was confirmed by Sir W. Thiselton Dyer,³ in association with Sir James Dewar, and was extended, by testing the effect of submersion in liquid hydrogen: germination was unimpaired in either case. The seeds selected by Dyer were of the commonest kinds: *Brassica alba*, *Pisum sativum*, *Cucurbita pepo*, *Mimulus moschatus*, *Triticum sativum*, and *Hordeum vulgare*.

But when all this has been said, there remains one fundamental difficulty in accepting the doctrine of an interplanetary bacterial panspermia; and that is, the lethal action of the solar light- and ultra-violet rays. Bacteria in the fully dried state, if free in the interplanetary vacuum, would be killed. And as Sir James Dewar's experiments have

¹ *Proc. Roy. Soc.*, 1900, lxvi, pp. 180, 339, 488.

² *Proc. Roy. Soc.*, 1898, lxii, p. 161.

³ *Proc. Roy. Soc.*, 1899, lxx, p. 361.

demonstrated that the ultra-violet rays will kill undried bacteria whilst in the frozen condition, at the temperature of liquid air (-195° C.), there is little left to support the Arrhenian hypothesis, that the living protoplasm on the Earth originally immigrated from interplanetary space in a free or uninclosed condition—that free, particulate life has entered the Earth's atmosphere as a result of light propulsion, from extramundane space.

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The Council think it right to state that the Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Surgical Section.

November 14, 1911.

MR. CLINTON T. DENT, President of the Section, in the Chair.

Case of Caries of Frontal Bone and Intracranial Abscess due to *Bacillus typhosus* Eleven Years after Attack of Typhoid Fever.

By W. RINGROSE GORE, M.B.

THE patient, an officer in the Army, now aged 31, contracted typhoid during the South African War in 1900. He had been inoculated on board ship five months previously, when he had a most severe reaction. His case was one of the worst recorded during the war. He was unconscious for five weeks, with a continuous temperature of 104° F., and was reported dead in despatches. On recovery he was invalided home, when he took a winter trip through the West Indian Islands, where he contracted malaria. Five years ago he was discovered to have albuminuria which has persisted to a slight extent. Four years ago an abscess formed over the lower third of the femur; this was opened in Egypt and after some time healed up. Subsequently the abscess re-formed and was found to communicate with the interior of the bone; it was operated upon again, and took a long time, eighteen months, in healing up. There is no record of a bacteriological examination being made on the first occasion. Subsequently an examination was made and a streptococcic and staphylococcic infection found. In the light of subsequent events this was most probably a typhoid abscess, possibly of the shirt-stud type, the typhoid bacillus

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being replaced by the later infection, as has happened in the present attack.

Last year he had his appendix removed during an attack of appendicitis. Last winter he had three attacks of illness commencing in November, each lasting a week, with a month's interval. The symptoms, which were similar in each, were headache, rigors, profuse sweating, and a temperature rising to 105° F., then complete recovery. No diagnosis was made.

I saw him on July 17 for a somewhat similar attack, a rise of temperature, slight and occasional headache not more than half an hour in the day, and then paroxysmal in character, slight and varying tenderness of scalp, and no other symptoms whatever, the patient feeling quite well: he had occasional night sweats, the temperature on the twelfth day reaching 103° F.

The urine contained albumin, but neither *Bacillus typhosus*, *Bacillus coli*, nor *Bacillus tuberculosis*, and the blood count was normal. At this period the case was an extremely puzzling one—there was obviously an infection, yet there were no localizing symptoms whatever. On the fourteenth day I found a small swelling in the scalp over the frontal bone in the middle line. I obtained some pus from this with a hypodermic syringe, from which a pure culture of *Bacillus typhosus* was grown. The abscess was then opened, and it was eventually found to be intracranial, the frontal bone having a hole about the size of a sixpence, and communicating with a cavity between the dura mater and the bone. The intracranial portion quickly closed up, but a sinus still remains leading down to the dura mater, brain pulsation still being felt. No dead bone could be felt.

The three attacks occurring during the last year must have been typhoidal periostitis going on to suppuration at the attack just described, although it is a characteristic of the late typhoid abscess that it can be dormant for some time without any rise of temperature or leucocytosis. The case is one of great interest owing to the very long interval between the original attack and the appearance of an abscess, the longest I can find recorded, although this year I saw one with a history of eight years between infection and abscess.

The important point now arises as to what can be done to prevent further attacks. These cases of typhoid bone infection coming on some years after the original fever are peculiarly persistent, one bone being attacked after another, the process going on for years. Although not usually fatal in themselves they may become so from their situation;

in my case, for instance, the abscess might have ruptured through the dura mater, and a case of fatal peritonitis has been recorded following a typhoid abscess of the lower end of the sternum.

One may take it that these cases are typhoid carriers, the habitat of the bacillus being in the walls of the gall-bladder, where they cannot be reached by medication or vaccines, as they are shut off from the circulation, but from which situation they can occasionally infect the blood-stream. Removal of the gall-bladder has been proposed and performed, but the operation in these cases appears to be a dangerous one. The other alternative appears to be to try by successive courses of vaccine to create a blood immunity. I had an autogenous vaccine prepared in my case. The largest dose I was able to give was half a million; larger doses produced too much reaction, showing great susceptibility.

In my case the pus from the abscess at first gave a pure culture of *Bacillus typhosus*; now this has disappeared, the pus containing *Staphylococcus albus* only. This is interesting as Janowitz has stated that a staphylococcic infection will kill off one of typhosus.

The result of a Widal test was reaction to a dilution of 1—200 only.

DISCUSSION.

Mr. C. A. BALLANCE said the case was one of great interest. He had never met with brain abscess occurring so long after typhoid fever as in Dr. Gore's case. He understood, however, that this was not really a brain abscess, but rather an intracranial one—i.e., outside the dura mater. He had operated on brain abscess following typhoid fever, but had never had to treat intracranial abscess from bone disease after such a lapse of time from the original disease. Only last week he saw a patient who had a very tender spot over a particular region of the skull, and who, fourteen months ago, had had a severe attack of typhoid fever in India. He thought that possibly the tenderness might be due to some latent typhoid lesion about to become active. This view, however, did not find favour with others who saw the patient. The account of Dr. Gore's case now confirmed him in the opinion he then formed, that in that patient already there was some residual typhoid osteitis, such as was sometimes seen in other bones, and that she probably had or would have intracranial abscess. The tender spot was over the occipital bone on the left side, and was exceedingly tender; it had appeared during the last three months. There was no œdema. The patient had never quite recovered

4 Gore: *Caries of Frontal Bone and Intracranial Abscess*

after the recurrence of the typhoid, and now the tenderness was increasing. At the time he did not propose to do anything, but he now suspected that something would arise which would call for operation.

Mr. BETHAM ROBINSON said the communication brought out very well a very important feature of the sequelae of typhoid—namely, their latency. The same characteristic was brought forcibly before one in operations on the gall-bladder, where in the bile or in the gall-stones typhoid organisms were found. Surgeons knew that there were many conditions, among which was perichondritis, that followed typhoid, and the interval was sometimes as long as five or six years.

Dr. GORE, in reply, said that in his case there was occasional tenderness of the scalp on pressure, but that pain had never lasted longer than an hour or so in the day. There was no pain at the actual spot where the bone perforated afterwards; there was no œdema. He examined the head every day, but the patient never felt anything more than an occasional slight pain in the head and some tenderness behind the ear. More frequently, the tenderness crossed over the frontal sinus, but there was no reason to suspect there was anything wrong there. Another case, which he saw this year, was also interesting. It was that of a youth, aged 21, who, eight years after typhoid fever, suddenly had a severe pain over the lower end of the radius. By means of the X-rays a necrotic area was seen. The pain continued until the part was operated upon. Mr. Lynn Thomas cut down upon it, and found a typhoid bone abscess in the lower end of the radius. It got well fairly quickly after the operation. This was the only other case of the kind he had come across. These typhoid bone affections were analogous to the old cold abscesses associated with tubercle, in which there was no disturbance at all.

Extraperitoneal Rupture of the Bladder without Fracture of the Pelvis.

By H. BETHAM ROBINSON, M.S.

INJURY to the bladder causing an extraperitoneal lesion is a much less common occurrence than one involving the peritoneal surface, and for this reason is worthy of record. Out of 169 cases of bladder ruptures collected by Bartels 49 were extraperitoneal, just under 29 per cent., while Fenwick makes the proportion as low as 12 per cent.

We usually associate a fracture of the pelvis with the extraperitoneal injury, and this does happen in the majority of the cases, but it must be borne in mind that a distended bladder may rupture in this position from a blow on the lower abdomen or even in a fall from a height. Instances are recorded of such accidents, and in the following case it will be noticed that one or both of these causes may have contributed to the lesion.

The history of the case is as follows: A man, a telephone mechanic, aged 43, was admitted under me into St. Thomas's Hospital on September 17, 1906. He had got up that morning at 4.30 and had then passed urine. When at his work, about 9 o'clock, he felt a desire to micturate, and on descending the pole for that purpose he fell 55 ft. He was only stunned for a few minutes and then the wish to micturate was increased. He had no recollection of any blow, but of course, under the circumstances this statement could not be relied upon. On trying to pass water he could not do so; there was marked pain down the urethra and in the lower abdomen, especially on the left side. Later in the day he was admitted into the hospital with still the desire to micturate and inability to do so. There was no evidence of any bruising or of a fractured pelvis (the absence of the latter was confirmed by X-ray examination); there was definite tenderness, most marked on the left side above the inner half of Poupart's ligament, and complaint of pain in this region. No lump could be palpated over the bladder area, but there was some increased resistance. There had been no bleeding from the urethra. There was no indication of any free fluid

in the belly. On using a soft catheter, which was passed without any difficulty, blood-stained urine was drawn off, but this came away without any force and only on expiration. No manipulation of the catheter brought away a further quantity. His temperature was 100° F., and pulse 88.

Examination thus pointed to an injury to the bladder, and twelve hours after the accident I operated. A midline incision in the bladder region disclosed a very marked infiltration with fluid, evidently urine, of the cellular tissue behind the recti. A metal catheter, easily passed through the urethra, came upwards in the loose tissue behind the pubic bones. Further exploration with the finger detected the bladder contracted down in the pelvis and displaced rather to the right. The peritoneal cavity had not been opened, but a large extraperitoneal rent was found in the bladder wall on the right side, starting just below the peritoneal reflection and extending downwards and inwards to end just above the neck, and it was at this spot that the catheter had left the viscus.

The position of the bladder made it very difficult to stitch up the wound in situ, and recognizing the desirability of leaving in a supra-pubic drain afterwards I made an opening in the midline of the bladder for that purpose and by passing my finger into it I was able to draw up the bladder and so facilitate and control the suturing of the wound. Six silk stitches were put in without piercing the mucous membrane and the wound was effectually closed. A Guyon's tube was inserted into the midline opening and the cellular tissue was cleaned with saline; a small drainage tube with a wick was passed down behind the pelvis and gauze drains were put in the cellular tissue on each side of the bladder.

During the next day (September 18) he was fairly comfortable; the temperature in the morning was 99·2° F. and at night 100·2° F., and the pulse 88 and 80. On September 19 the gauze drains and the tube were removed; his condition was good, without pain, and the bladder was draining well. From this time onwards progress was most satisfactory; the temperature, which for the first four days was slightly elevated, became normal, and his pulse was about 72. On October 1 he had passed urine through the urethra and the Guyon's tube was removed. For nearly a month there was a slight leak from the supra-pubic opening, but after that the wound was quite sound. For some considerable period afterwards I had him under observation and he had no further urinary symptoms.

In reviewing the above account the following points may be noted :—

(1) The position of the wound, which approached so closely the neck of the bladder without any associated fracture.

(2) The position of the catheter in the *cavum Retzii* and its relation to the neck of the bladder suggested momentarily the possibility of an intrapelvic laceration of the urethra at the apex of the prostate, with extravasation in the space, but against this were the absence of bone injury, the ease with which the catheter was introduced and blood-stained urine drawn off, the absence of urethral hæmorrhage, and, lastly, the collapsed state of the bladder instead of its probable distension.

(3) As to the operative procedure, criticism may be offered to making the second bladder wound and using suprapubic drainage. However satisfactory stitching with urethral drainage has proved in intraperitoneal lesions, we must bear in mind we have not such a good defence to our wound when the peritoneum is absent, and any hitch in the urethral drainage would cause increasing distension of the bladder, probable tearing out of the stitches, and recurrence of extravasation. For this reason alone the suprapubic drain seemed indicated. The bladder wound at rest had a much better chance of healing, whereas if it had given way a fistulous opening of long standing might have resulted. A positive advantage of the second opening was, as stated before, the control it gave in suturing the wound by the finger hooking up the bladder and at the same time being able to feel the depth the stitches were being placed in the bladder wall. Lastly, if this suprapubic opening had not been made and the upper part of the rent had been left open for the Guyon's tube the latter would have passed in too obliquely.

DISCUSSION.

Mr. L. A. DUNN said he was interested in Mr. Robinson's remarks as to the confirmation of the absence of fracture by X-rays. He had to deal with the case of a boy who, run over by a motor-car, had his pelvis jammed between the curb and the wheel. He had every indication of a ruptured urethra, and Mr. Dunn was able, by a good deal of coaxing along the roof of the urethra, to pass a catheter and tie it in. The patient was sent to the X-ray Department, whence he returned with a statement that he had not got a fracture of the pelvis. Mr. Dunn, therefore, examining *per rectum*, ran his finger along the rami of the pubes and satisfied himself of the existence of an irregularity, which proved to be fracture. He sent the patient back

8 Robinson: *Extraperitoneal Rupture of the Bladder*

with a report of what he had detected. The X-rays were then used with the patient in a different posture, and a very marked fracture was revealed. He had a case of extraperitoneal rupture of the bladder some years ago, in which there was found to be separation of the symphysis; it was not a fracture of the bone. Mr. Robinson described an extraperitoneal effusion of blood and urine. In his own case he let all that out by a suprapubic incision and drained by means of a large tube. He could not find the rupture of the bladder, but he did not doubt that if he had opened the bladder he would have found it. In that case the urine gravitated down to the left side and ran down by the side of the rectum, causing the left side of the rectum to slough. The whole pelvis was found to be packed with feces. He performed left inguinal colostomy and washed out the feces from above and below; the patient did well.

Dr. CAHILL thought it might be of interest to describe a case which he had had under observation some time ago, in which an extraperitoneal rupture of the bladder took place, between two and three weeks after fracture of the pelvis. In that case it was shown by the X-rays that the fracture of the pelvis was through the symphysis. In the early stages there were no bladder symptoms except inability to pass water, which had to be drawn off regularly. A fortnight afterwards, the patient not having yet recovered the use of his bladder, on passing the catheter to draw off the water as usual, the catheter became blocked, and on drawing it out a very large amount of slough was ejected from the urethra, about the size of the index finger. Examination of the material proved it to be a mass of simple sloughing tissue in an advanced stage of decomposition. Subsequently the patient had a urinary abscess on the right side of the pelvis which had to be opened and drained. This occurred about three weeks after the original injury. Thus the bladder had been pinched or injured at the time, had ruptured outside the peritoneum, and a considerable time after the injury an abscess had slowly formed in a few days. Subsequently healing took place and the patient recovered.

The PRESIDENT (Mr. Clinton Dent) said there were various points of interest and importance raised in the paper just read. He did not know what the experience of others might be as to such injuries, but it had always struck him that an injury of the bladder itself, whether intra- or extraperitoneal, was a curiously rare accident, apart from severe crushes, such as occurred when the patient had been run over, so as to call for surgical treatment. He could remember his old teacher Mr. Timothy Holmes expressing, year after year, the hope that before he died, or at least before he retired from the hospital, he might have the opportunity of having under his care a case of rupture of the bladder which required to be treated surgically. Curiously enough, a very few months before his retirement the opportunity came; the patient did perfectly well, although the condition was a very serious one. No suture of the bladder was employed. It was treated like a case of suprapubic cystotomy for the

removal of stone, and it was not then the custom to suture up the bladder wound. Mr. Dent had met with the injury but seldom in his hospital practice. The only recent case he could recall was one which must have been almost exactly like Mr. Robinson's, though brought about in a much more usual way. It seemed to be uncertain how the injury occurred in Mr. Robinson's case. In his own case the man received a blow on the bladder when it was full, and it ruptured extraperitoneally and very low down. It was not very long ago that, at a meeting in Hanover Square, Sir Thomas Smith threw out the suggestion¹ that the best and safest way to remove stone or growth from the bladder might be to cut into it intraperitoneally, not extraperitoneally, for one could then make certain of the wound healing up readily, and the sutures were less likely to break away or give trouble. If the bladder were lacerated extraperitoneally, this was more likely to happen. He did not gather whether, in Mr. Robinson's case, the wound in the bladder was in the midline, or to one side. Its position would have a considerable effect on the healing.

Mr. JAMES BERRY asked if Mr. Robinson would lay stress on the use of silk for the sutures; did he not think catgut would be better for a wound which might be contaminated by urine? He would like to know whether any of the stitches came away subsequently, or caused any other local trouble. It seemed to him that the suggestion which had been made, of opening the bladder and dealing with the rupture from within was an exceedingly good one.

Mr. BETHAM ROBINSON, in reply, said he accepted the statement of the radiographer that there was no fracture of the pelvis in his case. But he had also given his own experience, for he had had his finger behind the pubes, and the bone was thoroughly examined, and as far as he could make out there was no fissure; therefore he thought it might be definitely said that there was no fracture. With regard to the question of the President, as to whether the rupture was lateral, it was wholly on the right side. In answer to Mr. Berry's question, he simply stated the fact that he did use silk sutures, the reason being that at the date of the operation it was the usual thing in St. Thomas's Hospital to use silk; there was then great suspicion as to catgut. But times had since altered and catgut was now in fashion, and probably if he were doing the operation at the present time, catgut would be the material selected for the stitches. As far as he was aware, none of the stitches came out.

¹ *Med. Chir. Trans.*, 1901, lxxxiv, pp. 293-302.

Retrograde Enteric Intussusception.

By L. A. DUNN, M.S.

H. C., AGED 2, a Hebrew boy, was admitted into the East London Children's Hospital under my care on February 22, 1902, suffering from intestinal obstruction. The history was difficult to obtain owing to the fact that neither parent understood English, and the interpreter had only a very elementary knowledge of the language. It appeared that both parents were healthy, and that the patient was the only child. He had always been well till six days before admission, when he complained of great pain in the abdomen, and vomited. There had been great thirst, and when any liquids were given vomiting promptly ensued. The bowels had been constipated during the entire six days.

I saw the child soon after admission. He was lying on his back, pale and shrunken. The abdomen was distended and coils of intestine could easily be felt. Nothing in the shape of a tumour could be made out on palpating the abdomen. An enema which had previously been administered brought away some brownish fluid but nothing definitely faecal. On introducing the finger into the rectum the pelvis could be thoroughly explored, since, owing to the drowsy, collapsed state of the child little or no resistance was offered. The exploring finger encountered a sausage-shaped mass movable in the pelvis, to the right of the rectum. This could be displaced upwards, and was then detected by the hand which was palpating the abdomen. On withdrawing the finger from the rectum a little of the same brownish fluid was evacuated, but there was no trace of any blood-stained mucus and no putrescent odour about the fluid. Nothing abnormal could be detected in the rectum itself. There were no expulsive efforts on the part of the child until the finger had been introduced to its utmost limit.

The diagnosis of enteric intussusception having been made, the patient was prepared for operation. The abdomen was cleaned, the limbs were swathed in hot cotton-wool, and a large milk and water enema administered, which was promptly returned. Chloroform was given, and an incision made in the lower half of the right semilunar line about $2\frac{1}{2}$ in. long. The tissues were rapidly divided till the peritoneum was reached, and then a towel which had been wrung out of boiling water was held over the abdomen, so that when exposed the abdominal

contents should encounter a moist and hot atmosphere. This steaming process was continued by means of relays of towels throughout the entire operation. The peritoneum was then divided, and the finger, which had just been dipped into quite hot lotion, was inserted into the peritoneal cavity. The mass was soon discovered in the pelvis, and after some difficulty was delivered from the wound. The lower part, where the bowel was entering, was apparently tied down to the right iliac fossa, and could only just be dragged out of the wound, whilst the upper part was quite free. An attempt was made to reduce the intussuscepted portion by squeezing the gut above, but this was soon given up, as the ensheathing gut, which was composed of the small intestine, was found to be sloughing in one or two places. We then decided to resect the mass, so clamps were placed above and below. The lower clamp was difficult to adjust, owing to the very small portion of the gut there. The mesentery was ligatured in three or four pieces, and divided between the ligatures and the gut, and then the gut itself was cut across above and below the mass, between it and the clamps, and the portion thus freed was removed. As the gut above the upper clamp was a good deal distended, it was thought wise to empty it by removal of the clamp. This was done, and immediately a quantity of blood-stained fluid, of a markedly putrescent odour, escaped into a vessel held for its reception. One half of a small Murphy's button was rapidly tied into the cut end of the gut, and this portion was wrapped round with iodoform gauze. We then attacked the lower part where the bowel had entered, and there was so little working room that the lower clamp had to be removed before the other portion of the button could be introduced. Having accomplished this, the button was clamped together, and the gut thus united was returned after being washed with hot lotion. The abdominal wound was closed in the usual manner, and the child was wrapped in hot blankets and taken back to bed. The pulse, which was 156 per minute before the operation, had become almost imperceptible at the wrist, so strychnine was injected and several ounces of saline fluid were infused into the subcutaneous tissues of the axillæ.

After the operation the patient became very restless, sighing and yawning. The temperature, which was just below 100° F. before the operation, rapidly rose to 104° F., and the pulse became very feeble and rapid, so at 3 a.m. a pint of warm saline fluid was infused into the internal saphena vein.

The pulse now became stronger and could be easily counted, the rate being 160 per minute. The bowels acted several times, the motions

being dark, liquid, and some containing blood. Nutrient enemata with brandy were given every four hours. The temperature remained between 102° F. and 103° F. the whole day, and the pulse was still very rapid.

At 10 p.m. the temperature fell to between 99° F. and 100° F., and the pulse became almost imperceptible, so at 2 a.m. a second pint of saline fluid was injected into the other internal saphena vein. This pulled the pulse together, but the temperature promptly rose to 104° F., where it remained during the whole of the day; towards evening it reached 105° F., and the child expired at 10 p.m. The patient had thus lived rather over forty-eight hours after the operation.

Dr. Clive Riviere, Pathologist to the Hospital, reported upon the resected portion as follows: Resected piece. The intussusception was about 6 in. long, green, softening, and gangrenous. The large intestine was not involved, the inversion being of small intestine into small intestine. At the upper end appeared a small opening leading into a tube within the intestine, and on opening the innermost layer of gut a Meckel's diverticulum about 2 in. long was found, invaginated into the innermost layer of intestine and pointing downwards towards the advancing end. The intussusception was readily reduced, though there were recent adhesions between the layers.

Post mortem: The abdomen only was opened. The cæcum was adherent to the abdominal wall in flank. No general peritonitis. A piece of omentum adherent to the lower end of anastomosed gut. The anastomosis was performed by aid of Murphy's button, and was made just at the ileo-cæcal valve. The healthy appendix was almost touching the anastomosed gut. There was fibrinous exudation and adhesion between the opposed serous surfaces at the anastomosis. The junction appeared to be watertight, and no oozing has occurred. The cæcal end was injected and the peritoneal coat inflamed; the other end was more healthy. The ligatured mesenteric stump looked greenish and rather sloughy, but there was no peritonitis around it. The rest of the intestine appeared healthy. There was some gaseous distension of the small intestine, but very little faecal matter in the bowel. Liver: fatty patches; spleen natural.

The reason we diagnosed the condition to be one of enteric intussusception was the fact that, in addition to the vomiting and constipation, a sausage-shaped mass could be felt. The mass was clearly not in the colon or rectum, as it could not be discovered by external palpation, and it was only when the finger was inserted into the rectum that it

was discovered loosely hanging in the pelvis. Then the presence of visible coils suggested to our minds that the obstruction was higher up than usual in the alimentary canal. Again, the absence of blood-stained mucus passed *per anum* made us think that it had possibly been absorbed during its passage along a greater length of intestine than usual; this, however, was not the explanation.

We assert that the intussusception was retrograde, because, although at the time of the operation we did not see either end of the small intestine, we noticed that, when the mass was delivered from the abdomen, the lower end, the site of entrance of the intussusception, was so tightly tethered that it was difficult to adjust the clamp, whereas there was plenty of free intestine beyond the advancing end. When Dr. Riviere made the inspection, he noted that "the button was placed just at the ileo-caecal valve," and that "the caecum was adherent to the abdominal wall in the flank." This accounts for the difficulty we experienced in delivering the lower end of the mass where the bowel was entering. We were clearly working right against the adherent caecum. The gut beyond the advancing end of the mass could not possibly have been closely connected with the caecum, as here there was an abundance of small intestine which had to be replaced into the peritoneal cavity before closing the wound. Hence it is quite certain that what appeared to us at the operation to be the lower and entering part of the intussusception was really so, and therefore the intussusception was travelling upwards along the small intestine away from the caecum—i.e., in a retrograde manner.

DISCUSSION.

Mr. L. C. PANTING said he happened to have seen a case which he believed to have been a retrograde intussusception of the colon. He was without notes, and it was some four years or more since the case occurred. The patient, a girl, aged about 29, was admitted for a swelling in the right iliac region, the diagnosis of which was doubtful; there was no intestinal trouble, and it was considered to be ovarian in origin. On exploration he found an old salpingitis, and the colon, instead of lying in the usual position, was tilted downward and fixed in the pelvis, from which it ascended to the hepatic flexure. The caecum and appendix were normal. On separating the adhesions it was found that the colon was fixed to the upper part of the uterus and thence passed as the entering portion of an intussusception in a retrograde direction towards the caecum. He did a complete resection, but regretted to say that the patient died in some thirty-six or forty-eight hours from peritonitis. He had the

specimen in his possession, but had not thoroughly examined it, but so far as could be seen there was no growth. The narration of Mr. Dunn's case had brought it back to his memory.

Mr. BETHAM ROBINSON said it was very interesting to hear about the case because probably all surgeons had considered that the only conditions of retrograde intussusception were those which were seen post mortem. He did not wish to be critical of Mr. Dunn's case, but it did not seem to be certain that it actually was such a case. One knew the conditions that resulted from a persistent Meckel's diverticulum intussusception, and that might have been a factor in determining the condition of affairs in this case. Mr. Dunn drew attention to the fact that when he had examined the rectum there was a lump evident on the right side of the pelvis. This interested him, because twelve years ago he brought before the Clinical Society¹ a case of Meckel's diverticulum intussusception in which he had to resect the bowel, the patient being a boy, aged 5, and at the meeting he drew attention to a clinical feature of the case—viz., the feeling of a lump in the pelvis by rectal examination. He stated that although the symptoms pointed to intussusception, yet from that feature, and the fact that the lump was so low down and movable, and did not correspond to any sort of intussusception which he had previously felt, it occurred to him that it was probably a Meckel's diverticulum. This clinical feature seemed to be borne out now, and might be helpful in the future.

Mr. DUNN, in reply, said he was very much interested in Mr. Panting's remarks about his own case; it must have been very difficult to deal with in the large intestine. He supposed there was no growth. In answer to Mr. Robinson's question, there was no doubt about it being an intussusception. It lay quite close up against the cæcum. The advancing end was quite free, and there was plenty of intestine beyond.

¹ *Trans. Clin. Soc. Lond.*, 1900, xxxiii, pp. 12-14.

Surgical Section.

December 12, 1911.

Mr. CLINTON T. DENT, President of the Section, in the Chair.

A Case of Intestinal Obstruction following an Operation for Ovariectomy performed Forty-five Years previously.

By CLINTON T. DENT, M.C.

THE following case may be found to be of interest to the Section on account of its historical, as well as its clinical and pathological features.

A few years ago I was asked to see a lady, aged 69, who was suffering from intestinal obstruction. The history may be given in some detail: At the age of 23 she had been operated on by the late Sir Spencer Wells for an ovarian cyst. An increase in the size of the abdomen had been noticed for about three years. The increase had been very gradual, and the only symptom at all troublesome was shortness of breath. In the spring of 1863 she was seen by Sir James Paget, and in August of the same year by Dr. Charles West. The true nature of the disease was then first recognized and ovariectomy advised. Sir Spencer Wells operated in February, 1864. The case is described in his work on "Diseases of the Ovaries,"¹ No. 84 in the series. The operation itself was (in Sir Spencer Wells's own words) "as simple as possible. A non-adherent cyst of the right ovary was removed through

¹ The reference is to vol. i of a work by Sir Spencer Wells, published in 1865 (Churchill). It consists entirely of reports of 115 completed ovariectomies and a few incomplete cases. Case LXXXIV is the one to which this paper relates. The extract quoted is copied from the report on p. 216. No second volume of this work ever appeared. Wells's best known work, which bore precisely the same title, was published in 1872. It consists of much pathology, clinical work, and excellent descriptions of the operation and after-treatment, with a table of 500 cases.

an incision 4 in. long without any exposure of the intestines. There was no hæmorrhage. A pedicle of the breadth of two fingers, about 3 in. long, was secured by a very small clamp and fixed outside without traction." At that date, it will be remembered, the use of the clamp and the fixation of the pedicle to the abdominal wound was the customary practice. "The wound was closed by deep and superficial silk sutures. The left ovary was found to be healthy. The tumour removed was a simple one, and contained 16 pints of fluid. On the fifth day after the operation there was a slight tendency to prolapse of the pedicle, and the clamp was removed. On the eighteenth day the catamenia came on and 1 or 2 dr. of pus escaped just above the pedicle. The prolapse of the pedicle was now very considerable. It projected nearly 1 in. above the skin and extended laterally $1\frac{1}{4}$ in. On the thirteenth day after operation the pedicle was transfixed and tied doubly, the whole being secured by a third ligature. During the next week or two some flabby granulations around the pedicle were touched with caustics. The ligatures finally came away on the twenty-seventh day after operation. The patient was quite well, and there was apparently no further trouble."

"The cyst itself consisted of one large sac, and only one other cyst, very small and quite superficial, could be detected. The lining was smooth, shiny and velvety. There were no papillomatous growths." The report about the tumour was made by the late Dr. Wilson Fox.

The patient married a year or two later, and had ten children. Her health remained good. For a few years, however, before the attack of acute obstruction, she had had some intestinal troubles, at first constipation, but occasionally what was described as "diarrhœa." About three months before I saw her she had a decided attack of obstruction, and it was thought at the time that there was in all probability some commencing malignant disease about the sigmoid or pelvic colon. The attack, however, passed off, but she continued to have some trouble with the bowels. Four days before I saw her a second attack occurred accompanied by pain in the left iliac fossa. The obstruction was apparently complete, and no flatus had passed. There was a good deal of pain, and visible peristalsis, apparently of the colon, was noticed. Pressure on the abdomen relieved this pain. Enemata and aperients had practically no effect. There had been some vomiting, but only slight in character, and amounting to little more than the return of food. The vomiting was obviously gastric, and its reaction was acid. The patient was a very stout woman, and there was a great quantity

of fat on the abdominal wall, save over the scar of the ovariectomy wound, which was in the mid-line. At the lower part this scar was considerably retracted, the depressed portion of the cicatrix being dragged rather towards the left side. I did not, at the time, know the details of the former operation, and imagined that the pedicle had been brought into the abdominal wound, and had not become detached. There was only a moderate amount of distension of the intestines and the symptoms, in brief, were such as might be explained by a kink or compression of the intestines by old adhesions, or by an annular stricture about the pelvic colon. During the next few hours, although the distension did not increase, the pain became worse, and it was decided therefore to operate.

In such cases the best site for the incision is always a matter of some doubt. I elected to cut down in the left semilunar line, as I thought that it might be necessary to open the colon above a stricture, and I might have to deal with pelvic adhesions. The peritoneal cavity contained some serous fluid. A moderately distended small intestine, rather dark in colour, was at once seen. The colon was collapsed. It was at once evident that very numerous adhesions were present in the pelvic cavity, and these were evidently of long standing. Stretching from the neighbourhood of the sacrum, right across the lower part of the abdominal cavity, was a tough, tense cord, which terminated anteriorly in a cystic swelling attached to the lower part of the central abdominal cicatrix. The cyst was the size of a large orange. It could not be clearly seen, and I naturally assumed that it was an ovarian cyst springing from the left ovary, and that the slenderness of the pedicle was due to traction. This explained the depression that had been noticed on external examination of the abdomen. The uterus was small, deeply placed, slightly movable, and the pedicle could be traced down with the fingers to its left side. At the base of the pedicle were some soft adhesions which bled rather freely as they were broken down. The cyst separated away entire, fairly easily, from the abdominal wall. The pedicle was tied close to the uterus, and the cyst with its pedicle then removed. The pedicle had certainly acted as a cause of obstruction, but I could not judge of the extent to which it had interfered with the passage of the intestinal contents. The pedicle was not twisted, and the cyst, which was not opened at the time, appeared to contain only clear fluid. Numerous other adhesions, some of them due to appendices epiploicæ, were broken down, one of these being very tight and strong. This brought into view a long coil of collapsed small intestine, which was found to have been tightly constricted by old peritoneal bands in

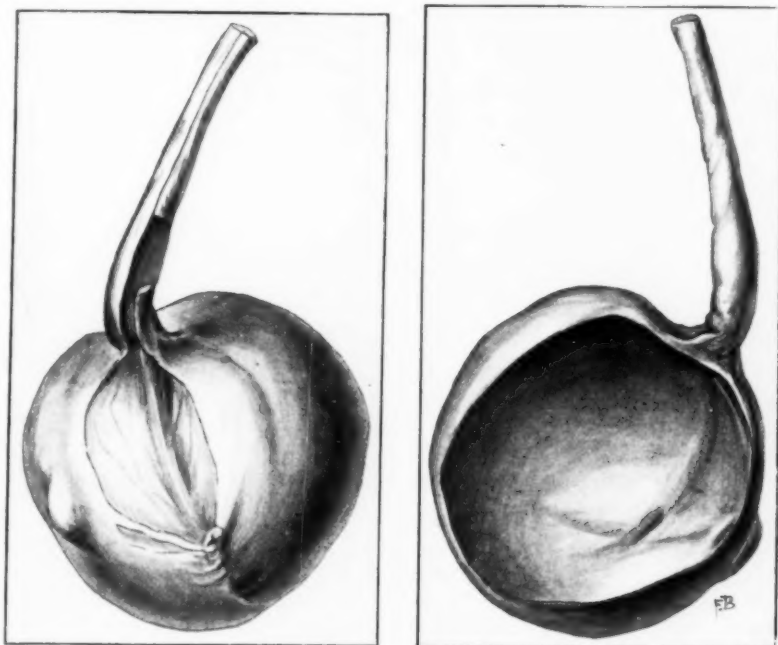
two places. By gentle stroking of the intestine the contents were made to pass on, and it looked as if this portion of the gut might reasonably be expected to recover naturally. The adhesions were so numerous that I could not make certain that every possible cause of obstruction was removed. The operation had been necessarily a prolonged one, and the patient was a bad subject for an anæsthetic. Moreover, there was a great tendency to protrusion of the intestines, although the distension was very moderate. At the lower part of the pelvic colon I could feel a hard mass within the bowel. This I took to be a mass of hard faecal matter, but it was not possible to feel certain that it was not a malignant growth. The large intestine was movable from side to side at this point, and this led me to think that the mass was due to faecal impaction rather than to malignant disease. The depth at which I was working rendered it quite impossible to get any view of the swelling. The large intestine down to this mass was quite collapsed, which rendered it further improbable, though by no means certain, that the mass was not malignant. No view could be obtained of the uterus. I imagined at the time that the left ovary, degenerated into a cyst, formed the adherent tumour. The left ovary was naturally not searched for. As so often happens in cases of the kind, the chief difficulty in the operation was experienced in sewing up the wound. The light had begun to fail, and as the room was lighted with incandescent gas lamps, and the patient was taking chloroform, the usual poisonous atmosphere was generated. Consequently the closing of the wound had to be done with all possible rapidity, and without any elaboration of detail.

The next day flatus had passed, and the condition was fairly satisfactory, though still very critical. On the fifth day after operation the bowels were got to act, and thenceforward the patient made a steady, though very slow, recovery. There was a good deal of ecchymosis about the abdominal wall in the neighbourhood of the recent wound, in all probability due to perforation of a large vein by one of the deep sutures. It became now fairly evident that the mass felt in the pelvic colon could not have been malignant, but was merely a very hard block of faeces. If I had lost sight of the case, as happens so frequently with hospital patients, I might have recorded it as one of recovery. Fortunately I was able to learn the brief subsequent history which, to my mind, is not the least instructive feature of the case.

Some two months later a further attack of intestinal obstruction occurred, but this again subsided. Four months after the operation yet another attack of obstruction commenced while she was away at the

seaside. I had no opportunity of seeing the patient during this attack. No operation was performed, the condition of the patient being thought too serious, and she died after twelve days from complete obstruction. No post-mortem examination was made.

The specimen is now in the Museum of the Royal College of Surgeons, No. 4557B, Old Catalogue. Mr. Alban Doran's description



Drawing of the specimen. (Natural size.)

is as follows: "A spherical thin-walled cyst 5 cm. or nearly 2 in. in diameter, to which there is attached a cordlike process of about the same length, which has been slit through transversely. Transverse microscopic sections show no epithelial lining, but unstriped muscle and vessels of relatively large size. There is no true lumen, the inner surface consisting of abraded muscular and connective tissue. This cordlike process is probably a Fallopian tube of which the lumen has undergone obliteration, the appearance of a lumen in the present

condition being simulated by the artificial slit made along its entire length."

The drawing made by Mr. Butterworth (*see figure*) shows the appearance of the specimen after preservation in spirit. There has been considerable shrinkage of the pedicle. As far as can be judged the extremity of the ovoid cyst was the part that was adherent to the abdominal wall. A curious tapering process of the cord extends over the wall of the cyst, which is seen to be very thin and uniform.

Mr. Shattock opened the cyst soon after removal and found it to contain a mass of fat and a quantity of hair which was of a reddish-brown colour. The cyst was therefore a dermoid, or teratoma. The pathology of this dermoid is, to my mind, rather puzzling. I think it is rather a conjectural explanation to regard it as possibly an implantation cyst connected with the former operation. I think one must assume that the left ovary was intact and that the cyst was not connected directly with it; but this does not agree with Mr. Doran's view that the pedicle of the cyst is a degenerated Fallopian tube of which the lumen has undergone obliteration. There was no trace whatever of a mesosalpinx. The pedicle was a small, fairly tense cord which stretched from the back of the pelvic cavity to the mesial scar in the abdominal wall.

If the pedicle were really a Fallopian tube, I think it must be assumed that it became attached to the abdominal cicatrix as the result of the ovariectomy, and that adhesions subsequently formed, gradually dragging the uterus backwards until it became fixed in the position it was found at the second operation. As the result of this alteration of position, the pedicle became elongated and stretched. There had been no pregnancy for, I think, over twenty-five years; but still the possibility that the case falls into the category of those in which pregnancies have followed double removal of the ovaries or removal of one ovary with disease of the other has to be taken into account. Such cases have been described by Mr. Doran in a paper entitled "*Pregnancy after Removal of both Ovaries for Cystic Tumour*,"¹ and are explicable on the assumption that some ovarian tissue was still present in the ovarian ligament. It seems pretty clear that no ovarian tissue was left behind at the first operation on the right side. I do not know, however, that any case has been recorded where so large a number as ten pregnancies have occurred.

¹ *Trans. Obstet. Soc. Lond.*, 1902, xlv, p. 231.

It is a matter of great regret that the actual state of the left ovary and of the broad ligament on the left side was never positively ascertained. There is thus a gap in the pathological evidence which cannot be filled up. It must be remembered that at the time of the original operation the left ovary was healthy.

A surgical point of the greatest interest to my mind is the formation of the adhesions. All the pregnancies, I understand, had been quite normal. There had never been any perimetritis or parametritis, nor had there been any illness that might have led to the formation of adhesions. I think, moreover, it may be taken as certain that there was no malignant disease of the large intestine, although the possibility of this had been suspected. On the other hand, there was a history of trouble following the ovariectomy and of suppuration about the pedicle which was fixed to the abdominal wound. My own view is that the adhesions commenced at this time, and they had persisted throughout the patient's life, though they had never given rise to any serious trouble. Adhesions of other serous membranes, such as the pleura, may undoubtedly persist for an indefinite length of time without even being suspected. In the case of the pleura they are less likely to undergo any material changes, but the free movements of the intestines and the alterations in the disposition of the viscera resulting from pregnancies will profoundly modify peritoneal adhesions. Some of them may disappear; others may become tougher until adjacent coils of intestine become firmly welded together or to the abdominal wall or other viscera; or the adhesions may become stretched, avascular, tough and string-like, according to the local conditions, and these changes may take place gradually and extend over a great number of years, never being suspected, until ultimately they lead, perhaps suddenly, to grave symptoms. The patient had been troubled with constipation for a good many years and this condition may have been partly or even wholly dependent on the presence of the adhesions; on the other hand, the constipation might have been quite independent of them.

All pathologists would, I suppose, agree that extensive intestinal adhesions are frequently found post mortem when there have been no symptoms during life to indicate their presence, and where there is no obvious post-mortem explanation of their original formation. They are certainly found, and not infrequently, where abdominal operations have been performed, although to all appearance the patient made an absolutely uninterrupted recovery without any complication at all. When a pedicle in an ordinary case of ovariectomy has been ligatured with silk,

the ligatures may come away years after the operation, and in such cases it is highly probable that some adhesions have formed. They may have disappeared again, but this is not likely, and indeed I think that after almost any abdominal operation, however uncomplicated and apparently complete recovery is in every respect, some intestinal or, at any rate, omental adhesions are usually present. Once present, they may persist; for the mere fact that adhesions are present is likely to lead to formation of further adhesions, so that, although some may disappear, others may take their place. Hysterectomy, particularly abdominal hysterectomy, is, I think, especially liable to be followed by the formation of extensive adhesions.

Recently, I had a patient who was admitted into the hospital with symptoms of intestinal obstruction. A year previously an abdominal hysterectomy had been performed, I believe, for uterine fibroids. The surgeon who operated kindly gave me information about the case. No adhesions, I understand, were found and the patient's convalescence was perfectly uninterrupted. The appendix, however, had been removed at the same time as the uterine tumours, but I understand that there was nothing amiss with it. When I saw the patient the symptoms of intestinal obstruction were very severe. An enormous number of adhesions were found all over the intestine, though they were most marked on the right side. Many of these adhesions were separated and divided, with the result that the colon, which was found very much collapsed on opening the abdomen, became more distended. It was impossible, however, to deal with all the adhesions, which were, as usual, largely omental adhesions. The patient died six days later, and post mortem a loop of small gut was found herniated through a gap between some adhesions deep down in the pelvis. There was also in another place a volvulus of the small intestine. Strangulation had occurred at both places. This portion of the gut was so bound down by adhesions and so matted to surrounding structures that elaborate dissection was necessary after removal from the body in order to demonstrate the condition, and it would have been quite impossible to have dealt with it surgically. In such cases, the commencement of the trouble is, I think, not improbably due to infection from the stump of the uterus. The peritoneum may be united over this satisfactorily, but still infection is likely to take place with the gradual formation of adhesions. Every surgeon has met with conditions of the kind, though the cases do not often enough form the subject of published communications. In such cases, even though the obstruction is relieved by operation on one or

more occasions, recurrence usually follows and the issue is ultimately fatal.

Two curious points are often noticed in these cases: (1) That although the patients have obviously had multiple peritoneal adhesions for many years, they may live in comparative comfort without the super-vention of any attack of acute intestinal obstruction; and secondly that when acute intestinal obstruction does occur, strangulation is so constantly found to be present in more than one situation.

DISCUSSION.

Mr. ALBAN DORAN said all present must have listened with great interest to the paper, which contained a high moral, namely, that all surgeons would do well to follow Sir Spencer Wells and Mr. Dent and report their cases fully. About six years before Sir Spencer Wells's best known work appeared in 1872 he published a book on about 120 cases, his first ovariectomies, every one recorded fully. Now a distinguished surgeon reported an after-history forty-five years after another operator of note had removed an abdominal tumour; but how many operations were unpublished before the patients came later on under the care of distinguished—and other—surgeons? In the olden days the clamp was the best appliance known. In this case the clamp was handled a good deal, and disastrous results ensued. Stilling, one of the earliest operators, lost several cases from tetanus when he used clamps. The pulling about in this case involved suppuration, and there were ten days of frequent handling of the parts. A pioneer, however, must have some bad results at first. The report implied that there was dragging on the intestine, and two or three adherent coils might have been drawn up against the wound. The duty of the second operator was, clearly, to relieve the obstruction, whether it came from a dermoid cyst, a common ovarian cyst, or a broad ligament cyst. Any tumour of those types might become twisted or adhere. Just as when a twisted pedicle atrophied, the tissues of the broad ligament and mesosalpinx became absorbed, leaving the Fallopian tube until the last, as it was the most resistant, so in this case, where the pedicle was dragged upon, the Fallopian tube had resisted better than the other tissues. He had seen a case where a small ovarian cyst had been hauled high up in the abdomen by the omentum, and there was an enormously long Fallopian tube, with the muscular tissue perfect, but the lumen obliterated. The other tissues of the pedicle had disappeared. That was the explanation of the present tumour. As the tumour was dermoid, it was evidently ovarian, and he believed it was the left ovary with its tube. The question had been raised whether the surgeon could guarantee that adhesions would not result after abdominal section, particularly when a stump was left behind. When the pedicle was let down into the peritoneal cavity—the usual practice at the present day—adhesions often developed. Many surgeons now

tucked in the stump behind the peritoneal cavity, and it was right to do so, especially after removing a suppurating tube. It was bad surgery to leave the stump in such a case bare in the peritoneal cavity. Still, if the stump was turned in under the peritoneum, or the uterus amputated entire, and the peritoneum sewn over the gap, a 4-in. or 5-in. line of sutured peritoneum was formed, and he did not see how, under such conditions, any guarantee against adhesions could be given. He would be glad if anybody could suggest any way by which the chance of adhesions could be reduced to a minimum.

Mr. DUNN asked how, if the tumour was a dermoid cyst, Mr. Doran would explain the ten pregnancies which the patient had after the ovariectomy.

Mr. ALBAN DORAN replied that dermoid elements did not preclude pregnancy. He had operated upon a pregnant woman in whom both ovaries were so affected, and on one side there was a very large dermoid. A dermoid, too, might develop in a year or two.

Mr. W. G. SPENCER said there was another class of adhesions which might cause the patient trouble, namely, those connected with fibromyomata which gradually atrophied and were supposed to come to a standstill, but the adhesions went on increasing. He had seen cases with such multiple adhesions, in which, whatever one tried to do, it was impossible to save the patient. He had had under his care a lady, aged 70, who years ago had a fibroid, and was told the disease would shrink. He supposed it did and that it had probably become calcified, but the adhesions had gone on, and there was an increasing tendency to intestinal obstruction, and that without any question of operation as a cause, as she had not had one done until that which he performed quite recently. A series of cases of adhesions had been reported after the use of iodine, and he thought it very important when using iodine in abdominal operations not to let the iodine touch the intestines; this increased the tendency to adhesions, not at first, but some months or a year afterwards, and the surgeon found it very difficult to deal with such adhesions.

Mr. MCADAM ECCLES said it was very rare to have ten pregnancies after removal of one ovary, and then to find a dermoid cyst of the ovary which remained. In view of a certain theory as to the causation of sex, it would be of considerable interest if Mr. Dent could say what was the sex of the children—whether they were all of one sex or not.

Mr. P. LOCKHART MUMMERY, discussing the prevention of adhesions after abdominal operations, said there were three points of importance. First, the wound should heal absolutely aseptically. Secondly, no surface uncovered by peritoneum should be left behind after the operation; in this he included leaving a stitch bare inside the peritoneal cavity. When operating with the view of leaving no adhesions behind, the peritoneal coat should show nothing but peritoneum; neither the stitches nor knots should be visible when the peritoneum had been closed. Thirdly, the operation should be done without any blood at all being left. He regarded blood, even in very small quantity,

left in the abdominal cavity as a very potent cause of subsequent adhesions. It was very easy to prick one of the tiny vessels beneath the peritoneum and cause a small hæmatoma to form; this seriously handicapped a successful result. If these precautions were carried out he did not think adhesions would occur after operation. Very careful technique was, however, required to secure a good result.

The PRESIDENT (Mr. Dent), in reply, said he could not give details as to the patient's children, but he knew they included both sexes. He agreed that the fact that she had had ten pregnancies was remarkable. He wished he had had more time at the operation and could have seen better; he had to judge largely by the feel. He believed there was still an ovary in the patient's abdomen. He thought Mr. Mummery's remark about blood left behind being a cause of adhesions was true; he was also sure that sometimes swabbing out blood from the cavity was a cause of adhesions forming, because the delicate surface was scraped in the act. Fortunately, such adhesions sometimes spontaneously disappeared. The formation of chronic multiple adhesions and their results was a point in practical surgery to which he thought sufficient attention had not been paid, and that was one of his chief reasons for bringing forward the case. Peritoneal adhesions were frequently a source of great trouble to the surgeon, but unless they formed, most abdominal surgery would be impossible.

The Radical Cure of Hernia in Infants and Young Children.

By THOS. H. KELLOCK, M.C.

THERE is probably no operation in the surgery of children that has come more into practice during the last few years than that for the cure of inguinal hernia, and rightly so, I think, for I hold very strongly the view that all of these are congenital in origin, as far, at any rate, as the sac is concerned, and that the only "acquired" factor is the protrusion of some viscus into an already existing sac. I think, too, that the removal of this congenital deformity is the proper course and the only course if a cure, in the proper sense of the word, is to be brought about. One hears of, and apparently sees, cases that are said to have recovered spontaneously or to have been cured by the application of a truss, yet I believe in these cases an unoccupied sac remains, only waiting for some unaccustomed internal pressure to bring about what one so frequently sees, the sudden, almost painless occurrence of an inguinal hernia of some considerable size in a young adult.

How operations for hernia have increased in number is shown by the statistics of the Hospital for Sick Children, Great Ormond Street, for I find that whilst in the year 1898 eighteen operations for this condition were performed, in 1910 the number had risen to 369.

In common, I expect, with most other surgeons, I think an operation can, and should, be done at an early age. As to the nature of the operation that gives the best results there would seem to be some difference of opinion; for my own part, for several years past I have reduced it to the very simplest form that I thought would answer the purpose.

The test of the efficiency of any operation for this condition can only be made by investigating the results some years subsequently, and in order to see what these results had been in some of my own cases I recently, with the help of my late house surgeon, Mr. C. Bryan, made an investigation into a number of cases, which proved to be of considerable interest. From the Hospital registers we took seventy-five cases which had been operated on from two to four years ago. We did not go further back because it was only about four years ago that I began to perform the simple operation which I shall presently describe. To fifty

of these cases we sent postcards asking the mothers to reply on them as to whether there had been any return of the rupture; whilst to twenty-five who lived within reasonable distance of the hospital letters were sent asking them to come and be seen. To the fifty inquiries we had twenty-eight replies; three of the children had died since the operation, two of pneumonia and one of peritonitis fourteen months after the operation; one had left the country. In each case the statement was made that up to the time of death or emigration there had been no return of the hernia. One mother stated that there was a bulging when the child coughed. (This case was sent for and seen subsequently; he had some weakness of the abdominal muscles on both sides, above and outside the inguinal canals, but there was no sign of any protrusion through the inguinal canal itself.) In all the other cases the reply was that there was no return of the rupture, and on nearly all the postcards there was some expression of pleasure or gratitude at the success of the operation. Of the twenty-five cases that were asked to come and be seen fourteen presented themselves, and in every one of them the cure seemed to be absolutely satisfactory. So that in these fifty-two cases, after the lapse of from two to four years one may claim that a satisfactory result had been obtained in all of them. The ages of the patients at the time of operation varied from a few months to 8 years, five were under 1 year old, eighteen between 1 and 2 years, seven between 2 and 3 years, and smaller numbers at the succeeding ages. In six cases the condition was bilateral, and the operation done on both sides at the same time.

I attach considerable importance to what may be called the preparatory treatment in these cases; when an infant has a hernia of any size that comes down easily, I have him kept for a few days before the operation in the Trendelenburg position. It is quite easily managed by fastening the feet and legs over a wedge pillow, and it is rather wonderful how soon they become accustomed to the position. After a few days the hernia rarely, if ever, makes its appearance, and when it has not been seen for a day or two the operation is done and the child returned to the same position again for another five or six days.

As to the operation itself, I generally make a 1-in. incision through the skin at right angles to the direction of the spermatic cord and just above the external abdominal ring; this incision is well away from the genitals, and being on the line of the blood-vessels is accompanied by very little bleeding; then dividing the coverings of the cord longitudinally the sac is found, thoroughly isolated, drawn down with a little force,

transfixed, and ligatured as high up as it can be reached, and the skin wound closed, my aim being to remove the sac, the whole sac, and nothing but the sac.

The operation is perhaps not quite so simple as this description sounds, and requires a good deal of care. The sac itself is generally thin and easily torn, especially at its upper part, and the vas deferens is always very closely attached to it. The separation of the vas from the sac calls for great care; it should be pushed off and not torn off, for in doing the latter a pinch with dissecting forceps is enough to seriously injure it, and this has been the cause, I believe, of those troubles in the testis which are sometimes said to follow an operation for hernia in quite young children. When a child's hernia is known to have been of some considerable size it is advisable, I think, at the time of operation, to ascertain what viscus it is that has been in the habit of occupying the sac; and this, as a rule, is easily done, for whatever is in the habit of coming down into a hernia generally resides, so to speak, immediately inside the internal abdominal ring when it has been reduced. If, then, when the sac has been opened a pair of blunt sinus forceps are passed into the abdomen and made to seize whatever lies just inside, they will bring down in all probability the offending viscus, and if this proves to be, as is often the case, a tongue of omentum or the vermiform appendix, this should be removed, for it must help towards a cure if after the operation the child has nothing in the abdomen that has ever been down in the hernia. Of course, if the forceps brings down intestine, large or small, this is immediately released, and allowed to return into the abdomen.

DISCUSSION.

Mr. DOUGLAS DREW said his experience corresponded with that of Mr. Kellock. Of the hernia cases on which he had operated at the hospital he had not yet seen a single recurrence, though many of the patients came to see him for years afterwards. He always made the ordinary inguinal incision, and it was his practice to split up the external oblique to a limited extent. He thought one could be certain of getting to the top of the sac, and not leave a possibility of pouching. Only under very exceptional circumstances did he do a Bassini operation—i.e., when there was a very large hernia in a young child. He thought the best suggestion Mr. Kellock had made was with regard to the Trendelenburg position. In a young baby with a large hernia it would be a good thing to keep the child in this position, not only to reduce the hernia, but

to add to the celerity of the operation, which for a small child was a severe one. He had done the radical cure as early as at 5 months old. He believed it must require considerable practice to be able to perform Mr. Kellock's operation with any degree of security; the sac was so very delicate in a child that he liked to see what he was doing, rather than to draw the parts out through such a small incision as Mr. Kellock described.

Mr. JAMES BERRY considered that the paper was an excellent one, full of useful practical points. Like Mr. Drew, he envied Mr. Kellock the skill which enabled him to do his operation through an inch incision. He asked how much of the sac Mr. Kellock removed in cases of true congenital hernia. He thought it was perhaps not sufficiently well known that even in cases of strangulated hernia in young children the Trendelenburg position for an hour or two often led to spontaneous reduction. He was glad to hear both Mr. Kellock and Mr. Drew condemn the extensive Bassini operation which was so often done, he thought unnecessarily, for hernia in young children. In the past he had himself done the Bassini operation in such cases, but gradually he had abandoned it for the simpler procedure.

Mr. McADAM ECCLES said he thoroughly agreed with Mr. Kellock that practically every case of hernia in a child, whether male or female, could be cured by operation, and he further agreed with him on the matter of preparation. In an infant with a large hernia, a week or ten days' preparation beforehand, by correct position and by correct diet, had a great deal to do with bringing about a successful result, for it enabled the surgeon to operate through quite a small incision, measuring at the most $1\frac{1}{2}$ in. He could not quite follow Mr. Kellock in regard to the position of his incision, but he agreed with Mr. Douglas Drew that the best incision was over the inguinal canal cutting through the aponeurosis of the external oblique, so as to expose the actual spot where the sac was in continuity with the parietal peritoneum; and it was sometimes easier to separate the sac from the cord there than lower down. He only transixed at this place the neck of the sac while it was on the stretch, and divided it after ligature. He did nothing more; he did not attempt to make anything like a tunica vaginalis.

Mr. DUNN said when he was on the active staff of the Shadwell Hospital many radical cures for hernia were performed, and he was in the habit of doing three in the hour. What he then did was a modified Kocher's operation. He thought that in Mr. Kellock's operation a small pouch would remain in the upper part of the funicular process which might lead to a recurrence of the hernia. He separated the sac from the tissues of the spermatic cord by means of blunt dissection right up the inguinal canal, and then pulled the sac up, and out, through a small hole in the oblique muscles, above and external to the internal abdominal rings. A ligature was then applied tightly around the sac quite close to the external oblique aponeurosis and the sac removed. The free ends of the ligature were next threaded on needles and passed under the

margins of the hole in the external oblique and tied, thus burying the stump of the sac, and at the same time closing the opening. He never saw a recurrence, and he thought cases so treated would always do well. There was a tendency for congenital hernia in an infant to get well if a truss was applied. He had seen many cases which were trussed for four years, and in which the hernia had not recurred. But admittedly it was better to perform the radical cure.

Mr. P. LOCKHART MUMMERY agreed as to the importance of doing a simple operation in the case of children with hernia. The only modification he had made on simple ligature of the sac was that after ligaturing the neck of the sac he threaded the ends of the ligature on to a curved needle, passed that needle under the external oblique, and brought it through the tissues rather above the level of the internal oblique, doing the same with the other end of the stitch and then tying them so as to draw up the neck of the sac. This caused a kink in the end of what was previously the entrance to the sac and helped to obliterate it. It did not occupy more than half a minute longer, and did not mean any extra suture. He did not leave sutures in the wound, with the exception of the ligature on the neck of the sac. The difficult cases were those in which a truss had been previously worn. When a child had been wearing a truss for two or three years, one found on dissecting up the sac that there were adhesions, and separating a thin sac from tight adhesions was very difficult. Curiously enough, he recently saw a case of recurrence at the Queen's Hospital for Children—the first case of recurrent hernia in a child which he had seen. It was a large recurrence with the sac down into the right side of the scrotum. He inquired carefully into the case to find out what had happened: the operation had been done by one of the house surgeons a year and a half previously, and a study of the notes of the case made it evident that there was considerable suppuration following the operation, so that it could scarcely be regarded as a recurrence in the proper sense of the term.

Mr. V. WARREN LOW remarked that the common factor in all that had been said was the non-recurrence of hernia in children, and he thought it stood prominently out that whatever one did in the way of operation on a child's hernia, except for such cases as Mr. Mummery had just mentioned, the tendency was for them not to recur. He believed in doing a simple operation, but Mr. Kellock's description did not give him the impression that the operation he described was the most simple, because it was difficult to separate the sac after it had left the external ring, in comparison with the ease with which it could be separated in the canal. It did not appear that any harm was done by making an incision into the external oblique. He did not hesitate to do so and to stitch it up afterwards. He would like to know the youngest age at which Mr. Kellock performed the operation. He agreed that it was advisable to operate for the condition in young children, but sometimes there were objections to operating on quite young babies—e.g., the difficulty of separating the child from its mother.

Sir ANTHONY BOWLBY, C.M.G., said that whereas a comparatively few years ago it was accepted that in almost all operations for the cure of inguinal hernia canal sutures were required, such had not been advocated by anyone in the present discussion. So far as small children were concerned, he had never used those sutures, and he had extended his practice in that direction to the larger number of cases of hernia in young adults—i.e., up to the age of about 25 years—in whom the hernia has not made progress towards the scrotum and spoiled the canal. He thought it was evident that the real abnormality in these people was that they were possessed of an open process of peritoneum which they ought not to have, and if that process was removed they became the same as other people. Therefore he thought the custom of not using canal sutures might be extended beyond the age of early childhood. Another point on which he would like to offer a remark was as to whether these children were really cured by a truss when they appeared to be cured. That was a question which it was very difficult to decide. The operation for the radical cure of hernia was comparatively recent, whereas the treatment of the condition by trusses was very old, and he thought it would not be fair to assume that everybody with hernia in childhood who had worn a truss, and was apparently cured, necessarily had a hernial sac which was patent for the rest of his life. In one case he had the opportunity of ascertaining that the hernial sac had been obliterated. He had to deal with a child who had inguinal hernia, and he advised that operation should be done, but the parents were loth to agree to that, and, to meet their objection, a truss was worn. He saw the child at the age of 2, and there was still a hernia, and he told the parents that if the hernia still persisted it ought certainly to be cured by operation. At the age of $4\frac{1}{2}$ they permitted the operation, and he then found a tunica vaginalis, but he had difficulty in finding anything higher up; and on extending the incision he found only a cord, which he could follow up from the tunica vaginalis. He could find no trace of an open sac in the upper part of the inguinal canal, so that, even though that child had a hernia at 2 years of age, there was no patent sac when he operated at the age of $4\frac{1}{2}$. He did not think many children would be cured like this one, after the second year, but he believed that not a few children were cured by a truss when it was applied quite early in life. This was, however, a belief the accuracy of which it must be difficult to prove.

Mr. KELLOCK, in reply, expressed his pleasure that his paper had induced such an interesting discussion. Although everyone had agreed that such hernias did very well if operated upon, his object in reading the paper was to show how well the children whose cases he had investigated had done after the simplest form of operation. Several of the speakers said their custom was to split the external oblique; he, personally, regarded this as bad practice, for in a child it was a congenital structure of good strength, which served a useful purpose throughout life, and he contended that one could not split the external oblique and sew it together again, so as to be quite the same as before.

In most adults who had recurrent hernia after the external oblique had been split, it was not recurrent inguinal hernia at all, but a ventral hernia into the scar which had been made at the operation. He also considered that putting a stitch through the sac and fastening it to surrounding parts was unnecessary; if all those children to whom he had referred got well without it, why do it? He was very glad to hear Sir Anthony Bowlby's remark about reducing the severity of the operation in young adults also. He (Mr. Kellock) was now, and had been for some time, doing an almost equally simple operation for young adults as for children, and he believed the results were as good as after the more elaborate measures. He believed it was a congenital defect, by curing which in early life one cured the hernia. Mr. Berry asked about the congenital sac; there was always a little difficulty with the terms "congenital hernia" and "hernia of congenital origin." If the sac of hernia included the tunica vaginalis, and so left the testicle in communication with the abdominal cavity, it must, whatever the operation, make that operation more complicated. He did not know in how many of the children he had mentioned the hernia was congenital, but in those cases it was necessary to separate the sac, and cut it across so as to leave a tunica vaginalis below. The principle of the operation was the same in these, though it took a little longer. He had used the preparatory treatment by position for many years, and it was useful not only for this condition but for double osteotomy. It was a great advantage to keep the children in the abnormal position for a little before doing the operation, for when they had become accustomed to that posture the after-treatment was much easier. In the case of recurrence which Mr. Mummery mentioned, he doubted whether the operator ever found the sac at all. With regard to the age at which he operated, the youngest in his list was 3 months old. He had operated for strangulated hernia at a considerably younger age. There seemed no reason why quite young infants should not have the operation done. He agreed that it was chiefly a matter of nursing, and provided that were good he did not see why there should be an age limit. He agreed that cures by truss were very difficult to prove. What one often saw in the out-patient department was a man of 25 years of age who would come in and say he had a hernia, which was reaching almost to the testicle. When asked how long he had had it, he would reply, a week or ten days, and that he had strained himself. Inquiry elicited the fact that after the strain he finished his day's work, and then found the hernia. He considered that it was a physical impossibility that a man, with so little inconvenience, could have a square foot or more of peritoneum suddenly forced down from his abdomen, for with such an accident there should be bleeding and pain; there must have been a pre-existing sac, although this was a fact that it would be very difficult to prove.

The Treatment of Claw-foot.

By ROBERT JONES, F.R.C.S.Ed.

IN the short time at my disposal I shall only be able to touch on the clinical aspects of claw-foot and on its treatment. I shall describe certain types, or rather degrees, of claw-foot, with which, I think, every surgeon has come in contact. The treatment of claw-foot is difficult; surgeons engaged in orthopaedic practice do not like to see these cases, and text-books do not give much information about this condition.

First, I would direct your attention to what I call "rectangular contraction" of the tendo Achillis, a condition which I regard as the first degree of claw-foot. In this condition parents bring the child with the complaint that he walks clumsily, stumbles often, especially when going up or down stairs, frequently tumbles when he is running, and that there is a want of "spring" in his gait. On looking at the child there is no visible deformity, but on examination it is found that the foot cannot be dorsiflexed beyond a right angle (right-angled contraction); if the child stands with his back to the wall he cannot raise his toes off the floor. It is this inability to dorsiflex the foot and ankle which makes the child fall over the front of his own foot. On following up a large number of these cases, I have found that many never get any worse, but others develop into typical cases of claw-foot. In these cases, as in cases of pronounced claw-foot, one rarely can get any definite history of any illness which could be regarded as an attack of acute poliomyelitis; indeed, it is very rarely that we find a typical form of claw-foot in patients who have had a severe attack of poliomyelitis, with definite paralysis of the anterior or extensor group of muscles in the leg.

The treatment in this early type of case is to elongate the tendo Achillis, remove nearly the whole of the heel off his boot, and put a bar $\frac{1}{2}$ in. thick across the sole just behind the heads of the metatarsals. This compels the patient to walk with his heels down and his toes tipped up.

The next picture is what I call the second degree of claw-foot. On looking at the foot the deformity is obvious. There is definite *cavus* or flexion at the mid-tarsal joint, the metatarso-phalangeal joints are

dorsiflexed, with the extensor tendons of the toes standing out prominently. The interphalangeal joints are flexed. The important point to be determined is whether the toes are at all rigid. The test for this is to place the tip of the finger under the prominent ball of the foot and press it upward; if the toes then relax into the straight position a good result will be obtained by the following simple operation: Subcutaneous division of the tense plantar fascia, followed by free wrenching to correct the deformity. As a rule it will not be necessary to divide the tendo Achillis. Subcutaneous tenotomy of the extensor tendons of the second, third, fourth, and fifth toes. Then make an incision on to the extensor proprius hallucis tendon and transplant it into the head of the first metatarsal by drilling a hole vertically through the bone, pulling the end of the tendon through it, and there fixing it. The extensor proprius hallucis is thus converted into an extensor of the mid-tarsal joint, and also lifts the ball of the foot under the first metatarsal head, correcting the deformity. The after-treatment is that of the first degree.

The next picture we have to consider is the third degree of claw-foot, in which the toes are rigid and do not relax when the ball of the foot is pressed up with the finger. The contracted bands of the plantar fascia are more conspicuous, and, in fact, all the features of claw-foot are more pronounced, and there is not much power in the muscles of the front of the leg (extensor group). The operation consists in dividing the plantar fascia and the flexor as well as the extensor tendons of the toes, for in such cases contraction of both groups is contributing to the deformity. The deformity must then be completely corrected by vigorous wrenching with Thomas's wrench until every resisting structure yields, and the foot can be kept in the straight position with ease. The case is now one of the second degree, and the transplantation operation already described may be performed.

The next picture shows what we may call the fourth degree, in which the deformity looks like a case of equino-varus. There are hard, painful callosities across the ball of the foot, and both the toes and the mid-tarsal joint are very rigid. In this, as in the treatment of all other deformities, all possible correction by wrenching and tenotomy should first be secured before proceeding to remove bone. Having got the foot into the best possible position, put it up in plaster in the fully corrected position for a fortnight, and then see what operation on bone is really necessary. In the case shown on the screen, at the second operation I removed a portion from the middle of the shaft of each

metatarsal, relieving the pressure on the heads of these bones, and then removed the astragalus, which allowed full correction of the tarsal part of the deformity.

A very terrible evil in bad cases of claw-foot is the intolerable pain of the callosities which form under the ball of the foot. The pad of fat between the heads of the metatarsals and the sole entirely disappears, and pressure ulcers may form, which have been mistaken for perforating ulcers. In these cases still more extensive measures must be taken. First comes preliminary division of all contracted tendons and fasciæ, with the best possible correction of deformity, then a fortnight later the astragalus and the heads of all the metatarsals are excised, thus removing the cause of the pressure callosities on the sole. Each extensor tendon is transplanted into the distal extremity of its contiguous metatarsal bone.

There is still one worse type, in which the patient has tried all sorts of treatment to alleviate his pain, and finally the foot and toes are rigid, without any movement, the callosities under the ball of the foot are huge, and pain is intolerable. The object of this paper is really to lead up to the treatment of these cases, and to describe an operation which I have performed in four cases only, but with very successful results. The operation consists in a preliminary correction of deformity by wrenching and tenotomy. At the second operation removal of the astragalus, which gives good play to the foot, is followed by amputation of all the toes, including the heads of the metatarsals, by means of a dorsal and plantar incision running along the bases of the toes. The extensor tendons are also transplanted into the metatarsals. The result is satisfactory, with a mobile ankle and no callosities in the sole of the foot.

DISCUSSION.

Sir ANTHONY BOWLBY, C.M.G., said it would be agreed that the cases such as Mr. Jones had described were among the most difficult which surgeons were called upon to treat. They commonly occurred in comparatively young men, whom they had unfitted for following their occupations, and many of the subjects of claw-foot had been refused for the police or the various services. It was evident that in the early stage of the condition something could be done to restore to the patient an efficient and painless foot. He quite agreed that there was a stage at which the patient was only too willing to part with the foot if amputation would result in relief of his pain, and if the operation now devised by Mr. Jones took the place of amputation it would leave the victim

with a very much better foot than he expected to have. He asked if Mr. Jones would, in his reply, give information on two points. Was it his experience, as it was Sir Anthony's, that most of the cases occurred in males? It would be of interest to hear the details of the operation which was performed in the earliest stage, because that was the time to catch these cases, and it was the stage at which many of the cases were seen.

Mr. DOUGLAS DREW asked whether, in an advanced case—one which would be suitable for excising the heads of the metatarsal bones—it was necessary to divide the tendons, both flexor and extensor, before doing excision of the heads of the metatarsal bones. He thought that would be unnecessary, as the shortening of the foot by removing the heads of the metatarsal bones would relax the tendons.

Mr. MCADAM ECCLES considered that cases such as Mr. Jones had described were the bugbear of the orthopaedic surgeon. They were exceedingly difficult to treat, and one almost gave them up in despair. What Mr. Jones had said was very helpful. He asked if Mr. Jones found any difficulty in the healing of these cases; in many of those at an advanced stage the skin became atrophic, particularly over the parts which had been greatly stretched, and sometimes, in his experience, sloughing occurred, although the parts had been kept thoroughly aseptic.

Mr. ROBERT JONES, in reply, said that in the earliest stage there was seldom any definite history of poliomyelitis. The foot was in a position of "rectangular contraction," and the child unable to lift his toes off the ground and to walk on his heels. The treatment consists in stretching, or, if necessary, dividing the tendo Achillis, removing the heel of the boot and putting a bar across the sole behind the metatarsal range and making the child practise walking. In the treatment of the next degree, after dividing all contracted tendons and correcting the deformity by wrenching, he fixed the tendon in a tunnel of the bone. Often he passed the needle and silk right out through the sole of the foot and pulled the end of the tendon right through the bone. In answer to Mr. Drew, his only reason for performing tenotomy of contracted tendons was to facilitate full correction of all deformity by the wrench, otherwise the toes contracted into a more claw-like position when the contracted structures in the sole were stretched with the Thomas's wrench. Even if he intended to do a subsequent open operation, he still divided contracted tendons to facilitate such preliminary correction as was possible. In the cases on which he had operated he had experienced no special difficulty in connexion with the healing of wounds, but had noticed that if any ulcer formed it was very slow in healing. Great care was necessary that there should be no bony pressure on the scar. In making his incision he was careful to go straight down to the bones and clear all the soft parts together, so as to get a good flap.

Surgical Section.

January 9, 1912.

Mr. CLINTON T. DENT, President of the Section, in the Chair.

The Operative Cure of Ascites due to Liver Cirrhosis (Talma-Morison Operation).

An Address Introductory to a Discussion on the Subject.

By RUTHERFORD MORISON, F.R.C.S.

THE first paper, published by Dr. Drummond and myself in connexion with this subject, appeared in the *British Medical Journal* of September 19, 1896. Not until Dr. Charles Frazier wrote on the "Operative Treatment of Hepatic Cirrhosis," four years later,¹ were we aware that anyone had a prior claim to our own in respect to the procedure suggested. As Professor Talma's suggestion and case were recorded in a Dutch journal and in the Dutch language, with which neither of us were acquainted, our ignorance will cause no surprise.

The first case, successfully operated upon more than sixteen years ago, was shown by me in the Medical Section at the annual meeting of the British Medical Association, in Carlisle, in July, 1896. The patient, after being tapped four times at intervals of a month, and then operated upon, had recovered her health, and was shown in excellent condition and without any fluid in her abdomen eight months after the operation.

In the first paper² I offered an explanation as to the manner in which the operation was suggested to me. During a visit to the post-mortem room Dr. Drummond showed me the body of a man dead from cirrhosis of the liver, and explained that this patient had

¹ *Amer. Journ. Med. Sci.*, Philad. and New York, 1900, n.s., cxx, p. 661.

² *Brit. Med. Journ.*, 1896, ii, p. 728.

no ascites because the collateral circulation, chiefly through the enlarged veins of Sappey, had relieved the portal obstruction. I then suggested that if his explanation were correct it might be possible to cure an existing ascites by an operation, which would establish a new anastomotic circulation. In the first case on which we tried the operation the ascites was not the result of cirrhosis, and the patient died nineteen months later, unrelieved.

The second and successful case was that of the patient shown at the British Medical Association meeting in Carlisle, previously referred to, and on which the paper (*loc. cit.*) of Dr. Drummond and myself was based. In this paper we first refer to the ordinary connexions between the portal and systemic circulations, and then say, "but when adhesions form between the viscera and parietes, innumerable new vessels develop in them and convey blood freely from the portal into the systemic circulation, through the subperitoneal plexus of veins." (The proof of this is that when a parietal and visceral adhesion are separated, both the visceral and parietal raw surfaces bleed.) "Probably the most important of these new channels can be developed in adhesions between the omentum and parietes.

A study of Nature's methods suggested that operation might be useful in selected cases, for we were familiar with the enormous newly formed blood-vessels frequently met with in the portion of omentum adherent to rapidly growing abdominal tumours; we had seen adhesions of all sorts in the abdomen develop large vascular channels, and we knew that such vascular adhesions could form with considerable rapidity. On one occasion one of us (Morison) removed an ovarian cyst with twisted pedicle of three days' duration, and already vascular adhesions had fixed the omentum to the tumour."

In a second paper on the same subject¹ I report the subsequent history of our successful case, and also the result of a post-mortem examination, as follows: "The patient, a woman, attended the Medical Section at the annual meeting of the British Medical Association at Carlisle eight months after the operation, and was then apparently in perfect health. The abdominal scar had yielded to some extent, producing a ventral hernia. This was the result of a cough which had troubled her for some months, and of imperfect suturing, but the hernia occasioned no inconvenience and was kept in place by an abdominal belt. Two years after the operation this patient called on me concerning her

¹"Cure of Ascites due to Liver Cirrhosis by Operation," *Lancet*, 1899, i, p. 1426.

ventral hernia. During this time she had felt strong and well, had led an active and happy life, and had performed all the duties of her household. Latterly a troublesome cough had led to a marked increase in the size of the hernia, and her belt had ceased to be a sufficient support. She was anxious to have the hernia radically cured, and, considering the trouble it was causing, the certainty that it would get worse, and the good condition she was in, I could not refuse to undertake the operation. (This was performed on October 5, 1897.) The only peculiarity observed was that the subperitoneal vessels were large and bled freely. She recovered in an hour from the immediate effects of the operation, but towards evening became restless, and complained of pricking pains and numbness in her arms and legs. Next morning, after a restless night, I found her distinctly jaundiced, and complaining still more of the numbness and pain in her arms and legs, which were very tender when touched. The jaundice and restlessness increased, and on the second day after the operation she became comatose and died at night, deeply jaundiced.

At the necropsy Mr. W. G. Richardson removed the whole of her abdominal viscera and the parietes, excepting the skin, *en masse*. He then injected the whole from the trunk of the portal vein. I showed the specimen at a meeting of the Northumberland and Durham Medical Society on November 11, 1897, and in demonstrating it, said: "The liver, the spleen, and the intestines are seen to be attached to the parietes chiefly by dense band-like adhesions. (Many of these seemed to contain little except a blood-vessel, and in several of them such vessel was 4 in. in length.) The omentum also is firmly adherent over the anterior abdominal wall by strong bands. In all of these adhesions innumerable injected vessels are readily seen, passing from the viscera to the parietes. Many of them are fully the size of a normal radial artery. The subperitoneal plexus of vessels forms a dense, large network. . . ."

Dr. Bolam reported as to the microscopical condition of the liver: "Typical cirrhosis with much fatty degeneration. Fibrous tissues well formed. . . . So-called new bile-ducts present in numbers, liver-cells showing extreme fatty degeneration in all zones, and normal cells few and situated in central portion of lobule."

This patient had a definite alcoholic history.

My second successful case, published in the same paper,¹ was that

¹ *Lancet*, 1899, i, p. 1426.

of a temperate man, aged 42, operated upon on January 12, 1897. His abdomen was much swollen and tense with fluid. "The abdomen was opened . . . between the umbilicus and ensiform cartilage, sufficiently to admit my index-finger for exploratory purposes. The characteristic hard, hobnail surface, which was felt on reaching the liver, left no further doubt as to the diagnosis, and the parietal incision was extended from the ensiform cartilage to the umbilicus. . . .

The general recovery of the patient requires no note. From the surgical point of view it was straightforward. It was, however, evident during the last few days of his stay in Newcastle that he was much depressed mentally, and after his return home the depression increased, and for three weeks he was alternately depressed and excited. This feature seems to be deserving of more attention than would have been given to the same in an ordinary case, for it may possibly be one of the special risks of this operation. Dr. Drummond has brought before the Northumberland and Durham Medical Society at various times cases of liver cirrhosis complicated by peculiar nervous symptoms, and in one patient who died he was unable to find any change in the nervous system to account for the symptoms. In that case the liver was in an advanced stage of cirrhosis; there was no ascites, and there was a very large vein of Sappey connecting the portal with the systemic circulation. The explanation given by Dr. Drummond of the attacks—viz., that they were due to intestinal products finding their way directly into the systemic circulation without any liver influence being brought to bear on them—is in accordance with the fact that this patient was on several occasions rescued from an apparently hopeless coma by the administration of a brisk purgative, and also with the results of experiments on the liver functions.

Subsequent history: Ten months after the operation my patient was shown at a meeting of the Northumberland and Durham Medical Society. He appeared then to be in excellent health and said that he felt perfectly well. . . . I next heard definitely of him in January, 1899. A well-known insurance office wrote asking me to report on the nature of the operation performed two years previously. He had been passed by the medical adviser of the company as a first-class life, but before completing the insurance I was consulted." This patient got pneumonia, of which he had previously had three attacks in the spring of 1903, and never satisfactorily recovered. He died of heart and kidney disease, with general dropsy and ascites. The post-mortem examination showed liver cirrhosis.

Tempted by this success I shortly afterwards operated upon an alcoholic man with cirrhosis and ascites who had never been tapped. He died three days after the operation, comatose and jaundiced.

The only other death I have had due to the operation occurred in a young woman on whom I operated in 1910. She had cirrhosis of the liver consequent on acute yellow atrophy, and had been tapped several times for ascites. She died three days after the operation, comatose and jaundiced, as the two previous patients had done.

My third successful case was published in the *Annals of Surgery*, September, 1903. The patient was a man, aged 52, a heavy drinker, who had been tapped before operation fourteen times for ascites, at intervals varying from six to twenty days. Operation (August 29,



FIG. 1.



FIG. 2.

Fig. 1.—R. P., three and half years after operation. Showing the enlargement of the epigastric vein on the right side. The wearing of a truss has prevented the enlargement of the corresponding vein on the left side.

Fig. 2.—R. P., May 4, 1910. A striking enlargement of the superficial veins, such as is shown here, may lead to erroneous conclusions. The circulation through them is relatively insignificant compared with that in the subperitoneal vessels. In many cases of cirrhosis the subperitoneal plexus forms a spongy sheet, which bleeds like a nœvus when incised. The object of operation is to make extensive communications between this and the visceral vessels. There must be, for this purpose, widespread adhesions. Operations which separate or excise the peritoneum should be avoided, and the omentum must be spread out and fixed under the abdominal wall.

1899): "The liver was firm, finely granular on the surface, and of about normal size. The spleen was hard and enlarged to at least double the normal size."

In July, 1903 (four and a half years later), the report on his condition by the surgical registrar, Mr. G. Grey Turner, is: "He is very

well; never looked better; is fat and strong and has a good appetite. There are no signs of fluid in the abdomen. The veins in the abdominal wall are very large. He complains of some dragging pain in the abdomen; the liver can be felt adherent to the abdominal wall."

In July, 1910 (eleven years after operation), this patient was shown to the Society of Clinical Surgeons of America, who visited this country. He had been doing regular work and was in good health. At the present time, between twelve and thirteen years after the operation, he is still well, and is aged 65.¹

In my last paper² I say: "Other factors besides mechanical obstruction of the portal vein doubtless aid the development or retard the arrest of ascites due to cirrhosis; but my cases prove at least that the establishment of an artificial accessory circulation can cure it." Further experience has confirmed this view, but, as I have always been careful to point out, the cases in which operation can be of use are rare and must be carefully selected.

So far as I know, the most suitable are those of alcoholic cirrhosis in patients otherwise sound, and whom repeated tapping has failed to cure. None of these cases have, in our experience, been failures. The reason probably is similar to that of the cure of dropsy from heart failure following persistent overstrain. In both the chief predisposing cause of the dropsy can be removed, in the case of the heart by rest, in the case of the liver by abstinence from alcohol. This explanation seems probable, because though I have operated upon patients in good condition with ascites due to syphilitic cirrhosis, none of them have been cured.

The most unfavourable cases are those which at their commencement simulate an abdominal emergency and suffer from pain and tense tympanites preceding the development of ascites.

THE OPERATION.

The choice of an anæsthetic may be of importance. The great danger in these cases appears to be the development of a condition related to acute yellow atrophy; and chloroform, as is well known, can produce similar changes in the liver, so that some other anæsthetic should be chosen.

¹ The same day my colleague, Mr. Grey Turner, showed a similar case. It is now more than five years since he operated, and the patient is well.

² *Annals of Surgery*, 1903, xxxviii, pp. 361-66.

My first case taught me that the abdominal incision should be made above the umbilicus to avoid the development of a ventral hernia. With this exception the operation I do now is the same as that I originally suggested. The steps are:—

- (1) Open the abdomen from the ensiform cartilage to the umbilicus.
- (2) Introduce the hand into the abdomen and project a finger against the anterior parietes in the middle line, 3 in. above the pubis.
- (3) Make a small incision on to the finger-tip, and through this introduce a long, small glass drainage-tube into the recto-vesical or recto-uterine pouch.
- (4) Dry the abdominal cavity and scrub the peritoneum with mops.
- (5) Suture the omentum to the anterior parietal peritoneum, across the abdominal wall, and close the upper abdominal wound.
- (6) Apply an antiseptic dressing over the wound and tube, and over this, from above down to the tube, a series of long, circular strips of adhesive strapping, with the object of keeping the parietal in contact with the visceral peritoneum.
- (7) The tube now exposed through the dressings is surrounded with a sheet of dental rubber, perforated to grasp it below the collar on it, and the separated tube dressing is wrapped up in the india-rubber sheet.

AFTER-TREATMENT.

A nurse is engaged to attend to the tube and pump off the fluid sufficiently frequently to keep the dressings dry. If this can be accomplished the dressings require no change for ten days, after which, as a rule, a small india-rubber tube can be made to take the place of the glass one. I have heard of septic peritonitis resulting from this operation. We in Newcastle have never seen this, and it may be that our free use of antiseptics during the operation and in the dressings is the explanation.

As a rule the wounds are entirely healed in one month, and no further accumulation of fluid occurs. It need, however, occasion no serious disappointment if the fluid re-accumulates, as some of our most successful cases have required tapping on one or two occasions after their recovery from the operation.

Many successful results have now been recorded from this operation, but I have thought it more fitting to occupy the time you have kindly placed at my disposal in dealing with the general principles involved, than in enlarging upon details which can be better treated by those who may take part in the discussion.

DISCUSSION.

Dr. HALE WHITE said that if he criticized the paper, it must be regarded as only a friendly criticism, and criticism added generally to the interest of a debate. Mr. Morison and he were agreed on the main point—namely, that the cases in which the operation under discussion could be applied were very rare. The next point on which they were in agreement was that there were probably other factors leading to the effusion of the fluid in the peritoneal cavity, besides pressure on the portal vein. If one paid attention to the cases brought forward that evening, it would be noticed that they were all more or less exceptional. The first case certainly was exceptional. It was unusual for a woman with cirrhosis to have ascites and not to become jaundiced for some years afterwards, and then die directly after the jaundice supervened. The second was not an alcoholic case, and the man had heart and kidney disease as well. And the fourth case was exceptional, because there was acute yellow atrophy in association with cirrhosis. The fifth case was also exceptional, for the man was tapped fourteen times, a most unusual thing in alcoholic cirrhosis; he had only a finely granular liver, and in spite of the operation he still went on drinking and living. These cases indicated that if the operation under discussion was going to be of use, it could only be so in a limited number of cases. With regard to uncomplicated alcoholic cirrhosis of the liver, the operation would be used less and less, for that disease would become rare, since the consumption of alcohol was notably declining. And it was probably not recognized that ascites was a comparatively rare symptom of cirrhosis, because in any large general hospital half of the cases of cirrhosis found in the post-mortem room had not presented any symptoms during life attributable to the cirrhosis; and of the other half which presented symptoms only half had ascites, so that only one-fourth of all the people with alcoholic cirrhosis had ascites. Our knowledge of the symptoms and morbid anatomy of this disease would scarcely lead us to think that the operation would be often useful, for it was a common thing in alcoholic cirrhosis of the liver for the ascites to develop quite suddenly. Sometimes within a few days the abdomen might be filled with fluid; he had seen such a case that day; and it was difficult to understand how a slowly contracting fibrous tissue would produce such a sudden effusion of fluid. It was not uncommon at a post-mortem examination to find a very atrophic liver with no

ascites. There was no great relation between the degree of cirrhosis and the ascites. Although in the first case which suggested operation to Mr. Morison the venous collateral circulation was well marked, yet everyone would agree that one might find in the post-mortem room cases with cirrhosis and ascites, but with the veins not particularly distended. Another reason which made it unlikely that the operation would be often used was that it was difficult to produce ascites in animals by causing pressure on the portal vein. A moderately tight ligature of the portal vein did not lead to effusion of fluid into the peritoneal cavity. A tighter ligature would lead to some fluid being effused, but it was almost as quickly re-absorbed.

To understand cirrhosis of the liver it was necessary to have a wider conception of the disease, looking on it in the same way as on granular kidney. It was true that the most obvious change was in the liver, but that change was produced by some poison, very often alcohol, but sometimes not alcohol; this poison circulated in the blood, as in the case of uræmia, and caused particular symptoms. The poison was a lymphagogue, because many of the cases of cirrhosis of the liver had swelling of the feet. This was not due to pressure on the vena cava by the liver, nor to pressure of fluid, since there might be no ascites, and the patients acquired ascites because the poison was a lymphagogue. Also it was common to get pleural effusion. The case he saw that afternoon had pleural effusion on both sides, as well as effusion in the abdomen. Then, too, the temperature sometimes seen in cirrhosis might be toxic. Sufferers from cirrhosis also had nervous symptoms; indeed, apart from becoming jaundiced, it was notorious that the man with cirrhosis of the liver usually died comatose. No doubt he was poisoned. So taking a larger conception of the disease, and if we agreed that the main symptoms were not local from portal pressure, but were general and toxic, then the cases in which the relief could be obtained by anastomosis of the portal and general veins would necessarily be few. Another proof was that if one looked back in the text-books of medicine thirty or forty years ago, one would find all the great clinical observers were agreed that in uncomplicated cirrhosis of the liver the onset of ascites meant that the patient was almost invariably near his end. Murchison, Watson, Niemeyer, Fagge, and Wickham Legg, all said the same thing. He had taken twenty-two of the cases from Guy's Hospital, and found that the average duration of life after ascites first appeared in uncomplicated alcoholic cirrhosis of the liver was two months, and only two reached three months. These

figures had excited some criticism, and Dr. Campbell Thomson approaching the matter in a critical attitude, examined the figures from Middlesex Hospital, but arrived at the same result—namely, an average life of about two months. Dr. Ramsbottom, at the Manchester Royal Infirmary, was also sceptical, and at first said he did not believe the statement, but he ended his paper by saying that the statement was correct. Thus, in uncomplicated alcoholic cirrhosis of the liver, the onset of ascites meant that the patient was near his end, and therefore it was unlikely that the operation could be of much benefit. It would probably do the patient harm if the operation was very successful—i.e., if the anastomosis was prompt and very efficient—for it was known that in dogs, turning the portal contents into the general circulation was fatal, with the production of nervous symptoms. And in Mr. Morison's second case, nervous symptoms supervened after the operation. So if one were to get an ideally successful operation, the result of it might be to kill the patient. Some might say that what he (the speaker) alleged could not be true because there were cases of cirrhosis that had been tapped very many times. He only asked such people to withhold their judgment as to the correctness of the diagnosis until they had been present at the autopsy, because his almost invariable experience had been that some other associated cause, generally some form of chronic peritonitis, had been found to explain the ascites in such cases. People with chronic peritonitis could be tapped a number of times. He remembered a man who was tapped thirty-two times, 790 pints being drawn off, and a woman who had been tapped thirty-five times. Therefore, his contention was that the operation suggested by Mr. Morison must, a priori, have only a limited scope. With regard to his own practical experience of it, he confessed that in the few cases in which he had asked his surgical colleagues to do the operation, he had not been able to satisfy himself that it had added to the patient's life, and his surgical colleagues had now dropped the operation out of their ordinary routine procedure.

Mr. W. G. SPENCER said that if he differed from Dr. Hale White it would be because he had had no experience of the acute form of ascites rapidly running on to death. Dr. Hale White drew a distinction between ascites and ascites due to alcoholic cirrhosis. His remarks might apply with limitations, but a practical point against the latter part of Dr. White's statement was the great advantage of an exploration of the abdomen for the cases of ascites which had been repeatedly

tapped. After the appearance of Mr. Morison's first paper, physicians—Dr. de Havilland Hall, Dr. Murrell, Sir William Allchin, and others—had sent him (Mr. Spencer) cases, in some of which the great value of the operation had turned upon the exploration of the abdomen. Others had been definitely cases which came under the heading of those described by Mr. Morison. He would mention two or three cases in which exploration had been important. One, under Dr. de Havilland Hall, was tapped ten times, and after each tapping carefully examined, but nothing found until the abdomen was explored, when it was discovered that she had two small papilliferous ovaries, which were removed; the patient was shown some time afterwards at the Medical Society, the condition having been cured. The second was in a young man who was tapped; no explanation could be given until the abdomen was explored, when he found a contracted adherent appendix. After this was removed the lad got well and remained so. This was, no doubt, an exceptional case, but it was worthy of mention. A third patient was tapped several times and later drained. It turned out on exploration that the cause of her ascites was pelvic peritonitis traceable to a puerperal condition, and she was cured by fixing the omentum. He showed her at the Medical Society some time afterwards, and she had remained well. Another case of an obscure abdominal condition was under the care of Sir William Allchin. The patient was invalided by his firm as incurable. On exploration it turned out that his ascites must have been due to chronic inflammation of the duodenum with peritoneal inflammation around, and it was cured after the omentum had been fixed to the abdominal wall. He developed superficial veins, though they were not so marked as in the photograph Mr. Morison had shown. He was taken back by his firm after an illness of eight years.

He (Mr. Spencer) had fixed the omentum in atrophic cirrhosis of the liver, and the cases had been relieved from further tapplings, but they had remained in bed without general improvement until death. One woman had a liver half the normal size, and lived only five weeks. He had not lost one of these cases from the operation. Of the cases of hypertrophic cirrhosis of the liver he would not say they were cured, but they remained a long time without return of the fluid. Perhaps they did not all accord with Dr. Hale White's connexion of ascites with cirrhosis, but there was one alcoholic patient who had been tapped many times. She was a typical besotted old woman, who said she drank as much as she could get. She was shown at the Clinical Society four years after fixation of the omentum without any re-accumulation

of fluid. She afterwards developed carcinoma of the breast, which was removed. It recurred six months afterwards, and she died. At the autopsy, an anastomosis, such as Mr. Morison described, was seen, but there was no fluid. Her statement regarding the interval of four years was that she continued to drink as much as she could get, though perhaps that was not very much. One patient, under the care of Dr. Hall, was well for five years; he then returned and was tapped; this was followed by heart changes and he died. Another case was one which Dr. Murrell called a variety of Banti's disease. It was that of a girl, aged 25, who had inflammation of the lungs, followed by ascites and repeated tapings; she had enlargement of the liver and spleen. After the operation she was relieved for one and a half years, and went back to her work. Then she relapsed and after further tapings died. The post-mortem examination showed anastomosis. He could mention two other cases which were moderately favourable. In both the patients wished for something to be done to avoid being continually tapped. A case under Dr. Hall and Dr. Roger Smith, of ascites with hypertrophic cirrhosis of the liver, was that of a lady a little over 30, who had been seen by two physicians, one of whom gave her three months to live and the other six months. The patient was weary of the tapings, which were greatly weakening her, and she urgently wished operation. The first operation, done in 1909, was by Mr. Morison's method. That relieved her for nine months. When the ascites recurred and tapping again became necessary she desired a second operation. So he adopted Dr. Wynter's method of putting in tubes, one in each femoral canal, and they conducted the fluid into her legs, which had to be kept raised. Later those tubes got blocked with fibrin, and the fluid re-collected in the abdomen. She then decided upon a third operation, and as there was a movable kidney it occurred to him to decapsulate the movable kidney and dissect off a neighbouring piece of peritoneum. This operation again relieved her from the need for continual tapping. Later, at a fourth operation he adopted Mr. Sampson Handley's method, taking doubled strands of long silk and putting them from the pelvis through the abdominal wall up to the breast, axilla, and kidney. This had not cured the patient, but tapping was required less often. The other day she was tapped for the thirty-fifth time and her liver then reached down to the umbilicus. He did not know the cause of the ascites. In another woman he varied the operations. She had been improved for a time by the Drummond-Morison method, and thought so much of it that she wanted something

more done. At the second procedure he did what was first proposed by Mr. G. R. Turner, of St. George's Hospital—namely, scraping the liver very hard. That relieved the patient for a time. Dr. Peter Paterson, of Glasgow, had invented a method of putting glass buttons in the abdominal wall, and Mr. Spencer, at a third operation, relieved this patient for a time by inserting a button. A patient under Dr. W. G. Stone had ascites complicated by diabetes. He died five weeks after epiploexy in diabetic coma. Both the diabetes and ascites were due to the formation of pancreatic calculi. Dr. Stone injected the omental vessels and found that a good anastomosis with the abdominal wall had already occurred.

Mr. Spencer had never seen any harm come from these operations, and he was sure the patients' lives were prolonged. It was a procedure which surgeons should urge, for it incidentally brought about an exploration of the abdomen.

Dr. H. D. ROLLESTON, after expressing his appreciation of the paper, said that he was in favour of the Talma-Morison operation in special and carefully selected cases, but that he did not agree entirely with Dr. Drummond and Mr. Morison that the multiplication of vascular peritoneal adhesions did good solely by increasing the anastomotic channels between the general and the portal venous systems and so facilitating absorption of the ascites. While believing that ascites was mainly toxic and not primarily due to increased pressure in the portal vein, he considered that the two mechanisms which Nature had adopted in order to compensate for cirrhosis of the liver were, first, mechanical, increased anastomosis, and, secondly—and on that point he wished to lay stress—compensatory hypertrophy of the liver substance. Mr. Turner and he¹ put forward the suggestion that the Talma-Morison operation not only increased the collateral circulation, but by improving the conditions of the hepatic circulation, partly by diminishing the engorgement which must interfere with its functions, and partly by increasing the blood-supply to the surface of the liver, it (1) enabled the liver to deal more satisfactorily with the smaller quantity of blood passing through it, thus diminishing toxæmia and the tendency to ascites; and (2) favoured the process of compensatory hypertrophy of the liver cells. In support of the latter contention he pointed out that in some of the cases in which the operation had been performed, and in some other cases in

¹ Rolleston and Turner, *Trans. Med. Soc. Lond.*, 1900, xxiii, pp. 63-9.

which cirrhosis of the liver had become latent and in which multiple adhesions had been found, as in a case recorded by Dr. Parkes Weber, compensatory hypertrophy of the liver had been well marked. To recapitulate, the Talma-Morison operation not only relieved mechanically, but it also enabled the other natural compensatory process—namely, hypertrophy of the liver—to take place. The Talma-Morison operation was therefore on a different plane from the other operations, such as those which consisted in draining the peritoneal cavity into a pocket, containing some omentum, beneath the abdominal wall (Narath's operation), or draining into the femoral canal (Wynter and Handley), or connecting the peritoneal cavity with the saphena vein (Routte's) operations. These procedures drained the fluid from the abdominal cavity.

Ascites had recently been treated in Paris by injection under the skin of ascitic fluid just withdrawn from the abdominal cavity (auto-therapy), a procedure which had previously been adopted for tuberculous pleural effusion. Possibly some of Dr. Wynter's cases benefited in the same way. He did not know whether this was in virtue of a contained vaccine, or whether it acted by altering the osmotic pressure and so allowing the absorption of the ascitic fluid. A very important point about the Talma operation was that the cases should be carefully selected, and operated upon early, almost as soon as ascites was definitely present. The most suitable cases were those in which ascites came on shortly after hæmatemesis, in which the patient was in good condition, and in which there was sufficient liver substance to enable compensatory hypertrophy to take place. Patients in the last stages of cirrhosis should not be operated upon, as they were prone to die, the end being hastened by the operation. The contra-indications to the Talma-Morison operation were: an advanced stage of the disease, the existence of grave cardiac or renal disease, and the presence of considerable jaundice.

With regard to the significance of the onset of ascites in cirrhosis, there was no doubt that the onset of ascites was often a late event and was comparatively soon followed by death. A distinction had been drawn by Dr. Hale White between cases of ascites due to cirrhosis, which did not live long enough to require tapping more than once, and cases of ascites occurring in cirrhosis but due to chronic peritonitis, which might require many tapplings. Dr. Rolleston believed that, granting that ascites was in the main a toxic process, the persistence of ascitic fluid in the peritoneal cavity would cause some degree of chronic peritonitis in virtue of toxins contained in the effusion. In other words,

the presence of some chronic peritonitis in a case of hepatic cirrhosis which had required tapping several times did not prove that the peritonitis caused the ascites; the chronic ascites might cause the chronic peritonitis. If this interpretation was true, the prognosis of ascites due to cirrhosis was not so grave as it would otherwise appear to be.

Dr. ESSEX WYNTER remarked that the ultimate causation of ascites was so broad a question that he could not touch upon it. The problem as it presented itself to him was that numbers of patients were detained in the sick room by the constant presence of a benign effusion into the peritoneal cavity, which required repeated tapplings, and which resulted in a condition in which the fluids taken by the patient passed almost directly into the peritoneal cavity, and the system itself was starved. This was borne out by the experience of the few days following an ordinary paracentesis for ascites, for one would find scarcely 10 oz. of urine as the daily output. He thought it was the starving of the body of fluid which was largely responsible for the toxæmia which commonly ended life. He was much interested in Dr. Hale White's statement with regard to the duration of life of a patient with cirrhotic ascites, because he had been met with derision when he stated that a patient with cirrhosis of the liver who developed ascites rarely survived five tapplings or more than two or three months. The general mass of the profession did not believe it, and he thought this due to a great lack of discrimination in the causation of ascites. The operation which he suggested to his colleague, Mr. Sampson Handley, for draining the ascites was based upon two principles: (1) relief of abdominal tension, and (2) supply of fluid to the system. It appeared to him that the development of collateral circulation was hindered by the tension of the abdominal wall due to the bulk of the contained serum. He thought Mr. Morison's success in the operation he had devised was rather due to continuous drainage of the peritoneum for two or three weeks, which gave an opportunity for the development of collateral circulation, than to the amount of anastomosis which might arise from the insertion of the omentum into the abdominal wall, this being absolutely trifling compared with what naturally existed. He had constantly noticed at autopsies in cases of cirrhosis of the liver that one of the largest conduits by which the blood left the abdomen was a great development of the lower end of the vena azygos major. He had frequently seen two branches as thick as the forefinger below

the diaphragm, and he thought considerable anastomosis developed in this region. In effecting relaxation of the abdominal wall by frequent or continuous external drainage, one was depriving the patient of an important nutrient fluid which was needed for the functions of the body and the excretion of urine. He thought, therefore, it would be much more valuable if that fluid could be retained and distributed through the body instead of being wasted. On that account he got the surgeon to open the femoral ring and carry the fluid into the subcutaneous tissue. He selected that point because of its convenience; it was a well-known route to the surgeon in dealing with femoral hernia, and it allowed drainage at the lowest available place. In the fourth case he had to deal with, he tried the insertion of a silver eyelet into the peritoneum of the anterior abdominal wall. It was of a larger lumen than the spool shown by Mr. Spencer, and would admit an ordinary cedar pencil. It answered well for drainage, but the patient developed a large abscess, and ultimately died. He thought the introduction of foreign bodies was liable to have this effect. The main difficulty in bringing about the drainage was due to the natural tendency of the peritoneum to close itself in a short time. He recently had a case in which, owing to a defect in suturing the wound, the patient was kept in the horizontal position for three weeks. The fluid drained satisfactorily into the leg, but when she got up he found she had a pouch the size of two fists in the upper part of the thigh, which practically limited the fluid. He believed this was due to the development of an endothelial lining to a subcutaneous pouch, formed by the fluid which was hindered from diffusing. It was the only case he had had in which such a thing had happened. He believed that success depended on relieving the tension of the abdominal wall, and at the same time supplying the system with a certain amount of fluid. If the patient was going to be drained by removing the serum from the body, fluid should be supplied by injection under the skin; it was no good giving it by the mouth or by the rectum.

In conclusion, he thanked the Section for inviting a physician to speak; he hoped the alliance between the physician and surgeon was one which was growing, and that combined action would be more common in the future.

Mr. SAMPSON HANDLEY said that while fully admitting Mr. Morison's claims as the pioneer of the operative treatment of ascites, he was perhaps naturally prejudiced in favour of methods more recently

developed at the Middlesex Hospital, which began with Dr. Essex Wynter's suggestion of femoral drainage. It had been his privilege to carry that suggestion into practice. But he was prepared to admit that at present there was not sufficient material to decide between the conflicting claims of various methods. His experience taught him that operative treatment was only applicable to a minority of cases. In some cases where the fluid was secreted in almost a torrent all drainage operations were a failure. The methods used in the operative treatment of ascites belonged to two classes. In the first class were the methods which aimed at diverting the blood-current to the systemic system, and in the second those which acted by facilitating the absorption of the ascitic fluid. The former seemed at first sight the more rational method. But there were numerous natural anastomoses which were capable of being developed to form a collateral circulation, so that the addition of another channel by way of the peritoneum might not make much difference to the area available for the blood to flow through. The good effects of the Talma-Morison operation could be accounted for partly by the continual drainage of the abdomen, and partly because fluid was able to leak out by the side of the omentum into the subcutaneous fat. At any rate these were possible factors in addition to the establishment of a collateral circulation. Moreover, omentopexy had a danger of its own, that of toxæmia, from the diversion of an extra amount of portal blood into the systemic system. The second class of operations for ascites—those which acted by draining the ascitic fluid—contained at present four operations. He would not say any more about femoral drainage, as Dr. Wynter had already referred to it, but he thought it was the operation of choice for ascites, as it was simple and safe, and less severe than omentopexy. He had described its technique fully in his Hunterian Lectures on lymphatic surgery.¹ The second method was by silk drainage (lymphangioplasty). He had done this on three occasions. The first was a success.¹ The patient was operated upon more than two years ago, and when seen recently was well and at work. It was a case of cirrhosis, which was partly alcoholic and partly syphilitic. He laid a number of silk threads from the peritoneum of the iliac fossa to the thigh, and sewed up the incision in the peritoneum with thick silk, so that the fluid could leak along the silk sutures into the subcutaneous tissue of the abdomen. At first

¹ W. Sampson Handley, "The Surgery of the Lymphatic System," *Brit. Med. Journ.*, 1910, i, pp. 853, 922.

the operation seemed to be a failure. She had to be tapped on one occasion, but since then she had not required it. She still had some fluid in the abdomen, but not enough to interfere with her occupation, nor, indeed, with her resumption of alcoholic habits: she was still drinking. Mr. R. Atkinson Stoney had recently recorded a successful case of lymphangioplasty for ascites. Silk drainage should be employed in cases where femoral drainage had failed, and where the ascites collected at only a moderate rate. The third method was that of forming a communication between the internal saphenous vein and the peritoneum. He was surprised to hear that this had been done. He tried it himself on one occasion, but as it was a failure he did not record the method. He hoped the valves of the saphenous vein would be competent, but the vein persisted in bleeding into the interior of the peritoneum, so he had to tie it off and own himself beaten. He hoped the surgeon referred to by Dr. Rolleston had had better success. There was still another possibility—namely, to unite directly the internal saphena vein to one of the branches of the portal vein. Recently he saw an account of an operation by this method in Dublin, but he could not remember the reference. The case was not a success, but as suture of blood-vessels became better understood he hoped the method would prove an ideal one, although there would be the danger of turning a good deal of portal blood into the systemic system. With regard to auto-serotherapy, he continued to see references to that subject, but it was worth remembering that it came from the same country as the N-rays. He asked any physician who had opportunities of tapping ascites to try auto-serotherapy and record the results; it would be very easy to inject some ascitic fluid into the subcutaneous tissue.

Dr. F. PARKES WEBER said his attention was first drawn to the matter in 1898 by making a post-mortem examination¹ on a man, aged 44, who had been, several years previously (in 1892), under treatment by Dr. Gee at St. Bartholomew's Hospital, where the diagnosis of cirrhosis of the liver with ascites was made. When the patient died, in 1898, the post-mortem examination showed that he had really had

¹ Dr. Weber reported the case in the *St. Bartholomew's Hosp. Rep.* (Lond., 1898, xxxiv, p. 321) under the heading, "Cirrhosis of the Liver—Effect of Peritoneal Adhesion in Arresting the Symptoms of Hepatic Cirrhosis." He remarked: "In favour of the view that the peritoneal effusion, for which the patient was treated in 1892, was of an inflammatory nature is the relatively high specific gravity (1020) of the fluid first drawn off, and the patient's tendency at that time to have fever in the evening."

cirrhosis of the liver, but that the paracentesis abdominis at St. Bartholomew's Hospital had been followed by the cure of the ascites and by the formation of extensive peritoneal adhesion. The man had evidently had chronic peritonitis in addition to his hepatic cirrhosis. Dr. Weber believed that a certain amount of chronic localized peritonitis was common in cases of cirrhosis of the liver, and he thought that it was better not to separate sharply cases of chronic peritonitis associated with cirrhosis of the liver from cases of hepatic cirrhosis without any chronic peritonitis, excepting in regard to the greater probability of peritoneal adhesions and new vascular channels developing in the former class of cases. With his surgical colleague, Dr. E. Michels, he (Dr. Weber) had had at the German Hospital four cases of chronic ascites, probably associated with cirrhosis of the liver, which were operated on for the cure of the ascites. In every case the result was successful, but in none of the four cases was omentopexy (a better term is "epiploexy") by itself sufficient, and in one case the omentopexy was altogether omitted. Before the operation the general condition of all four patients was fairly favourable, but each case needed repeated paracentesis abdominis, so that there seemed to be no prospect of getting rid of the ascites without some kind of operative interference beyond mere tapping. In the case of a woman, aged 42, whom he showed three years after the omentopexy, at the Clinical Section of the Royal Society of Medicine on May 14, 1909,¹ peritoneal drainage had been required to supplement the omentopexy. The same applied to a woman, aged 49, whom he showed at the same section on December 10, 1909.² He then remarked that in both cases the good result followed Dr. Michels's peritoneal drainage rather than the omentopexy operation itself. The moderate fever immediately preceding the disappearance of the ascites was a noteworthy point. He suggested that: "In regard to chronic ascites and the question of operative treatment beyond simple tapping, cases of hepatic cirrhosis might perhaps be roughly divided into the two following groups: (A) Patients who for some reason (for instance, the presence of old perihepatitis and perisplenitis and extensive spontaneous omental adhesions) have the collateral venous circulation well established, and do not readily develop ascites, but are especially liable to hæmatemesis from dilated œsophageal or gastric veins. The liver is generally decidedly enlarged in this group of cases. (B) Patients with a poor collateral venous

¹ *Proceedings*, 1909, ii (Clin. Sect.), p. 236.

² *Proceedings*, 1910, iii (Clin. Sect.), p. 80.

circulation, who develop ascites early. The main object of omentopexy and peritoneal drainage should be to convert patients of Class *B* into patients of Class *A*."

In the case of a London barman, aged 44, whom he showed at the Clinical Section on April 8, 1910,¹ omentopexy had been given up because, when the abdomen was opened, the omentum was found quite atrophic and could not be fastened to the abdominal wall; an attempt to fasten the spleen to the abdominal wall also failed, as it could not be brought down sufficiently. In that case the irritation due to the laparotomy was followed by irregular pyrexia and (after one further paracentesis) by the cure of the ascites, though the patient's enlarged liver could still be felt, reaching down to the umbilical level. The fourth case² was that of a woman, aged 46, on whom, in 1905, Mr. G. J. Jenkins performed the operation of omentopexy during the temporary absence of Dr. Michels. Paracentesis was necessary after the operation, and one of the tapplings (by the house physician at that time) was followed by intraperitoneal hæmorrhage and grave collapse. Dr. Michels, who happened to be in the hospital at the time, opened the abdomen (chiefly under local anæsthesia), cleared out the blood-clots, and ligatured two omental vessels which he found bleeding. The patient, in spite of her collapsed condition (for which normal salt solution and camphor dissolved in oil were injected subcutaneously), recovered, and the ascites, though it temporarily returned, did not again need tapping and was absorbed gradually. At one time some digitalis was given, and afterwards diuretin. In that case also a notable feature was the moderate evening pyrexia (up to 100° F. or slightly over) during the period of recovery from the ascites.

From these cases and other reports it seemed to Dr. Weber that an attempt at continual peritoneal drainage (in reality in *chronic* ascites the rubber tube or catheter used for the drainage tended soon to get blocked up), or some other kind of considerable peritoneal irritation, was generally necessary, in addition to omentopexy, for the cure of the chronic ascites in cases of hepatic cirrhosis. In one of the above cases the irritation of the laparotomy, together with repeated tapplings, sufficed without omentopexy. An inflammatory febrile reaction accompanied the gradual disappearance of the ascites in some cases. In the rare cases which had been reported of rapid cure of ascites following

¹ *Proceedings*, 1910, iii (Clin. Sect.), p. 167.

² *Trans. Med. Soc. Lond.*, 1907, xxx, p. 255.

the operation of omentopexy it seemed that the irritation of the peritoneum due to the operation was an essential factor in the immediately, or almost immediately, favourable result.

Mr. G. H. MAKINS, C.B., said he had had but a small experience of Mr. Morison's operation, and that had been obtained in operating on cases in conjunction with his colleague, Dr. Herbert Hawkins. Cases of alcoholic cirrhosis with ascites had been operated upon by him four times, and once with little ascites. The cases seemed worthy of mention, although the final results were not known in all of them. In none of the patients was albuminuria or jaundice present, and all had been tapped several times previous to the operation.

The first case was that of a man, aged 59, who had been ill for some months. The liver was scrubbed and the omentum fixed to the anterior abdominal wall. The abdomen needed to be tapped once or twice subsequently, but the patient steadily improved and left the hospital well. He remained well for two and a half years, but then began to drink heavily again. At the end of three years he was readmitted to the hospital with ascites and obvious enlarged anastomotic veins in the abdominal wall, and on that occasion both the abdomen and the pleuræ were tapped. After this sufficient improvement occurred to allow the patient to leave the hospital, and he had not since been heard of; as the operation was performed in 1901, the patient was probably dead.

In that same year a second patient of a similar class was operated upon, also a heavy drinker. When the abdomen was opened much ascitic fluid was evacuated, but the liver was very small, and the omentum was infiltrated as the result of chronic inflammation and rolled up into a ball. As the omentum could not be utilized, the upper surface of the liver was scrubbed and the organ itself fixed to the under surface of the diaphragm with stitches. This patient got well, and was seen in good condition between six and seven months after the operation; since then he had not been seen again.

The third case was of a similar class, and was worth mentioning because the patient died from a cause which had not been alluded to in others related. The man, aged 46, was in an advanced condition and had been tapped many times. The operation consisted in scrubbing the liver and fixing the omentum. On the third day the patient became restless, vomited first dark fluid, then blood, and in a few hours he died. At the post-mortem examination dark blood was found in the stomach, also diffused along the whole intestinal canal. He thought

it could only be supposed that the operation had something to do with precipitating the end, but the patient's condition before the operation was no worse than that of the others.

The fourth case was an odd one, and Mr. Morison had spoken of cases of the kind. The patient, a man, aged 39, came into the hospital as an acute abdominal emergency; there was distension of the abdomen, much pain, and evidence of some fluid in the flanks. The abdomen was opened on the supposition of acute inflammatory mischief. Two pints of fluid were evacuated, but nothing abnormal except a hobnail liver was discovered. In view of the condition of the liver, the omentum was sutured to the abdominal wall. It might be that in this case the development of ascites was commencing, but the man got rapidly well and had not been heard of since.

The fifth case was that of a man, aged 50, with a large cirrhotic liver and great ascites. The abdomen had been tapped several times. The operation again consisted in scrubbing the liver and fixing the omentum. Shortly after the operation the patient became very restless, delirious, and becoming comatose he died. The only special point observed at the post-mortem examination was the presence of acute nephritis, discovered on microscopic examination, although the kidneys did not appear much changed to the naked eye.

The five cases illustrated some of the difficulties and dangers of the operation, but he considered they were attended by sufficient success to justify the procedure in patients able to bear it.

Mr. SINCLAIR WHITE (Sheffield) sent the following précis of his experience and conclusions with regard to the Talma-Morison operation:—

"I have operated on nineteen patients and have had five deaths directly due to the operation; three from anuria with mild delirium passing on through coma to death at about the end of a week; one from septic peritonitis on the eleventh day, consequent on bursting open of the abdominal wound during a fit of coughing; and one from exhaustion on the fourth day in which there was free venous oozing from the omentum. Of the cases which recovered from the operation four were not appreciably benefited. In three cases the ascites did not completely disappear, but some improvement in health occurred; all three, however, died within twelve months from the date of operation. In the remaining seven cases the ascites gradually disappeared—in two of them not until subsequent tapping had been done—and a more or less

complete return to good health ensued. Unfortunately, in two instances a relapse to intemperate habits, in one patient after an interval of nearly two years, ruined what promised to be permanent recoveries. One patient is in robust health after an interval of nine years, a second was, a few months ago, reported to be quite well after an interval of nearly six years. A third died of carcinoma of the colon two years after operation without recurrence of the ascites. The two remaining cases have been operated on during the last twelve months, and both promise well.

“Operative measures should be restricted to: (a) Securing adhesions between the anterior surface of the great omentum and the posterior surface of the right rectus muscle. I make a 6-in. vertical incision, 2 in. to the right of the linea alba, reflect the peritoneum and posterior layer of the rectus sheath outwards and inwards; implant the omentum into the pocket thus formed, and secure it by a few interrupted sutures, taking great care not to puncture the omental vessels. (b) Peritoneal drainage through a suprapubic opening for from six to ten days. A progressive increase in the amount of urine excreted from the third day onwards nearly always takes place in patients who do well.

“From a surgical point of view cases of cirrhotic ascites may be conveniently divided into two classes. In one of these, owing to a well-developed anastomosis between the portal and systemic veins, ascites appears only as a terminal symptom, and not until the liver-cells are hopelessly damaged and there is present accompanying degeneration of the vascular and possibly renal systems. Patients of this class are rarely difficult to diagnose. The congested skin with spider-webbed angiomata of the face, often an icteric hue in the conjunctivæ, great loss of strength, rapid wasting of the upper half of the body, acute progress of the ascites with œdema of the legs and genitals, and pronounced dyspnœa and tachycardia on slight exertion, are the sure harbingers of death which no operation can avert. In the other class the collateral circulation is imperfectly developed, and ascites, of gradual onset, appears as a comparatively early symptom, before the hepatic cells have undergone serious degeneration. In many of these it would appear that the incidence of the poison (alcohol or other) extends to and is most marked on the peritoneal covering of the liver, hence an extensive and pronounced perihepatitis is commonly found associated with a greater or lesser amount of interstitial fibrosis. The patients are usually under the age of 50, may have quite healthy vascular and renal organs, and, apart from the abdominal distension, may be in fairly

good health. These are the cases which derive great benefit from epiploexy, and generally speaking it should be restricted to them. There are, of course, borderland cases where the expediency of operating will give rise to anxious consideration. When in doubt one or more tapplings will often help us to arrive at a decision. Indeed, in all cases a preliminary paracentesis is of value."

Mr. MORISON, in reply, said that after hearing the remarks of Dr. Rolleston and others he had crossed out the sentence from his paper referring to the operation having been neglected in this country. He was not aware of what had been done by some who had spoken, and he apologized for that paragraph. The most important of the problems which had been raised was as to the cause of the ascites. He had said that if Dr. Drummond's explanation, that the condition was a mechanical one, was correct, the operation ought to cure it. He did not himself believe that it was entirely mechanical, but the only part which was curable by operation was mechanical; the toxic element, always an uncertain one, could not be dealt with by the surgeon. All the results he had wished for had been achieved, and he regarded the discussion which had ensued as an excellent one; certainly he had learnt much from it, and he was much obliged to all who had participated.

Surgical Section.

JOINT MEETING WITH THE MEDICAL SECTION AND
SECTION OF ANÆSTHETICS.

February 13, 1912.

Mr. CLINTON T. DENT, President of the Surgical Section, in the Chair.

Partial Thyroidectomy under Local Anæsthesia, with Special Reference to Exophthalmic Goitre.

An Address Introductory to a Discussion on the Subject.

By T. P. DUNHILL, M.D. (Melbourne).

(Communicated by JAMES BERRY, F.R.C.S.)

ALL that I shall speak about to-day is the result of my own experience. The conclusions are such as I have been driven to. I shall not dogmatize if I can help it, because there is much room for legitimate difference of opinion on every aspect of the subject. When I began this work, partial thyroidectomy for exophthalmic goitre was regarded as being at least fairly dangerous, and the operation was not a frequent one. The number of cases which have now been operated upon enables one to speak with more knowledge, but we are still far from finality.

By way of introduction, I might say that I was led into this work in the following way: through interest in the disease, and reading the medical literature, I had been removing the thyroid glands from milch goats, and feeding the patients on the milk. Thus I had quite a number of patients under me in the outpatient department of the hospital. One day there came a patient who was exceedingly ill, who had no living relations, and who begged for any treatment which would

relieve her. After a little time I decided to operate, and placed the whole position before her. She wished for operation. I asked my senior surgeon (Mr. Murray Morton) for a bed. After the operation, other patients who had seen her in the outpatient room asked to see her in the ward. Then another asked to be operated upon. Ultimately all were operated upon. Since that time I do not think I have had to persuade a patient to undergo operation. The first lady is now cook in one of the largest provincial hotels in Victoria.

I shall not speak of aetiology. It seems to me that the chief interest to you will centre around such questions as, "Is surgical interference justifiable?" If so, at what stage of the disease is it indicated, and to what extent is interference desirable? Then comes the question of the absolute or relative safety of the patient, and what modifications of technique help to assure this? Finally, and most important of all—in what condition do we leave the patient?

I have written¹ that, judged from the point of view of response to operative treatment, cases fall into four classes:—

First, the classical type: There are present, goitre, tachycardia and palpitation, tremor, staring eyes, with or without exophthalmos. There may or may not be complete amenorrhœa; emaciation, alopecia, and other less constant symptoms. But we can detect little or no organic degeneration. The heart has not "broken down," if we may use that term to indicate either definite œdema of dependent parts or irregularity of pulse. It is arguable whether operation should be performed in this class or not. There is the possibility of complete return to health by medical treatment or rest, or with no treatment at all. Also there is the possibility that, in spite of all medical treatment, the disease may progress, to end either in death or in such organic degeneration that return to health is an impossibility. We will discuss that later.

Second class: In this class I place those cases in which the disease has progressed until there has been organic degeneration; and among them there have been some complete wrecks—irregular heart, œdema, enlarged liver. The existence of this class at all (and it is a comparatively large one) is some answer to the query as to whether cases in the first class should be operated upon; and it is certainly some answer to the statement still made sometimes, that all cases ultimately

¹ *Brit. Med. Journ.*, 1909, i, p. 1222.

get well if they live long enough. It has been stated that cases in this class are too far advanced for operation, I think for two reasons: (1) that they are too ill to stand the operation, and (2) because degeneration of organs has advanced to such a stage that improvement is impossible. We will discuss that also later.

Third class: In this class I place the cases in which the thyroid gland is quite small, in which it can sometimes scarcely be detected; and yet, associated with that small gland, there may be an extreme degree of one or more of the characteristic signs. There may be absence of tremor, or of exophthalmos, though either or both may be excessive. There may be smothering sensations or flushings. In spite of a rapidly beating heart the patient is usually over-fat, if one may use the term.

Fourth class: In this class I place the cases in which there are some thyrotoxic symptoms, associated with a goitre which is not truly exophthalmic in type. I do not mean by this cases of simple parenchymatous goitre, which have been in existence for some years, and have then become exophthalmic in type. Those are among the worst of cases. But there are some cases of adenoma of the thyroid in which the position of the adenoma behind the sternum or clavicle, or the adenoma, apart from any question of position or size, seems to irritate the surrounding gland tissue and cause some tremor, some staring of the eyes, and make the heart more easily excited.

To speak of the considerations which influence one in deciding whether to operate in each class, one has to take into account the position in life of the patient, and the severity of the case in relation to the progress made under medical treatment. If a patient has means and leisure, and the symptoms are not progressing, and one feels that there is no danger of the heart condition passing from mere irritability into organic change, then medical treatment could safely be persisted with for an indefinite time. Against this, one has found that again and again a patient has moved on from one practitioner to another, or has stayed away from her own practitioner, and ultimately comes back, with oedema of the feet. I will instance two cases. I recently operated upon a patient who had seen a practitioner in one of our larger provincial towns two years ago. She took his medicine for three months, then went to a Chinese herbalist. She took the drugs of the Chinese herbalist for one year and nine months; she then saw a medical man who sent her to me. This patient's sister had died in a hospital

from goitre years before. I think of another case, where a woman had been going along fairly well and seeing me at moderately long intervals. One morning she came with a heart enlarged, the apex well beyond the nipple line, and an irregular pulse. Some nights before she had gone to a dance; that, I presume, had been the culminating cause, though it is more probable that the trouble had been progressive before the dance. I myself refuse to operate until I know that the patient has had three months' efficient medical treatment, unless there are present other circumstances influencing the case, and one is guided by all the circumstances. One man, a sub-inspector in an insurance office, I kept under medical treatment for nearly twelve months, but he could never work with efficiency—always the thumping heart with the least exertion, and often without. At the end of the time I removed one lobe. Response to operative treatment in this class is very prompt, and the cure is complete if organic heart disease is not present, and if sufficient gland is removed. With local anaesthesia and expert operating the danger is *nil*.

In the second class one gets every stage of wreck—extreme emaciation, oedema, sometimes only in feet and legs, sometimes up the whole body, sometimes in the face if the face be low, as during sleep. Pulse irregular; apex-beat anywhere between the nipple line and the axilla. They constitute a class which most men who operate for goitre say should not be touched for two reasons: (1) because operation is too dangerous, and (2) because organic disease has so far advanced that improvement cannot follow. Out of 380 thyroid operations altogether, I have performed nineteen on cases in this class, and I say that operation is not too dangerous, and that very great improvement follows. One case, a patient of the President of the Victorian Branch, was lying on a bed utterly prostrated. She was oedematous; the stethoscope dented her chest wall; her apex-beat was 1 in. outside the nipple line. She had incidentally freely movable kidneys, a retroverted uterus, was almost blind (though not old), and whilst in hospital became deeply jaundiced. Dr. White assisted me to remove one lobe, and, later, half the other. She now leads a happy life, does light work, walks, and drives. Of course she cannot do hard work, and her heart can never be sound, but she was completely invalided before.

I have reported before (*loc. cit.*) the case of a nun, whose face was asymmetrical with oedema every time she slept. Dr. Shields helped me to operate upon her three years ago, and she has since been made

Mother Rectress of her convent. She says, with a smile, "That she cannot go up and downstairs *too* many times a day." Her pulse is irregular, but quiet; and she does her work fairly comfortably. Two patients whom I had placed in this class on account of œdema, and what was apparently heart failure, completely recovered; and each does all the female labour on a farm. I could multiply instances and details. All of these patients may be written to, or letters from them seen. I do not think that any anæsthetist would care to give a general anæsthetic to cases in this class, but under local anæsthesia one can state that the patients stand the operation well. There is only danger under two conditions: (1) operating under an acute exacerbation of poisoning; (2) operating when bronchitis is present.

About the third class, some authors say that even in the smallest glands associated with thyrotoxic symptoms one can detect the active part and remove it. I cannot, and I think it is unwise to remove portions of a gland which is not obviously enlarged, even though all, or most, of the other characteristic signs are present. One wants to be sure that there is no enlarged portion beneath the sternum or either clavicle. If there, it is not always easy to detect. Microscopically such glands show acini densely packed with active cells, and the activity of gland tissue per cubic space is so great that if half or two-thirds of the gland is removed the remaining portion is still so poisonous that it produces symptoms; and it seems that those densely packed cells are likely to atrophy from mutual pressure later. That is only opinion, but the few cases of this class that I have operated upon make me disinclined to remove gland substance.

The fourth class I will not take up time speaking about. The response to operation is immediate and complete.

I think that here I should speak of the mortality. That is one of the most important points to the physician who is deciding the welfare of a patient. I have published enough about the first case I lost, removing too much tissue at once with much crushing when one was inexpert; that was Case XIII. I lost my second case through operating when bronchitis was present, but the pulse-rate was getting higher each day, and the condition was grave; one took the risk to try and save life. Hypostatic pneumonia followed, and the patient died. The third case was moribund when I operated. She had been ill for some years and became rapidly worse; then she was sent up to me. Her pulse-rate was between 160 and 180; and she was acutely ill. With

Leiter's tubes and calcium lactate the pulse came down to 144 one morning, but rose again to the vicinity of 170 to 180. I knew I could remove the larger lobe rapidly. I thought that, even then, if the larger lobe could be removed without much handling it might not be too late. I discussed it with the husband; he could see that she was dying. I did it. It made no difference at all; the pulse kept the same for the next twenty-four hours, and she died. That woman had two years during which she could have been operated upon safely, and completely cured. The last exacerbation came on whilst she was under medical treatment; then it was too late. I have lost one other case, the circumstances surrounding which I cannot publish. That is four deaths in 380 operations of all classes, and in 230 cases of exophthalmic goitre, and for each death there was an accountable reason.

I think the opinion is becoming almost universal that under certain circumstances operation may be necessary in any case, but there are many who would regard it as being only a last resort. For reasons, some of which have revealed themselves as we have gone along to-night, I feel strongly that operation should not be regarded *only* as a last resort. So long as it is regarded as a last resort operation cases will be continually progressing from Class I to Class II, and the practitioner will have taken away from the patient her chance of complete recovery. Also I would like to say that during the last eighteen months five cases have been sent to me which simply died as soon as they got into hospital. Operation was out of the question; they were dying when they arrived, and all of them had been under constant medical attention. One came 160 miles by train, reached the hospital in the afternoon, and died the same night. One drove 20 miles in a conveyance, 200 miles by train, ambulance to a private hospital, and died. One died at home in the few days intervening between the time when she decided to come into hospital and the day when a bed could be ready. One was admitted into a medical ward until a surgical bed could be ready, had diarrhoea and vomiting all the time, and died before operation. One of the deaths I mentioned after operation might be added to this number, for she was practically moribund when she arrived, making the number six who were sent absolutely too late for surgical interference. That is one aspect of the *dernier ressort* view!

Then, when speaking of the permanent damage which may occur, I would mention one case in which the eyes were so proptosed that the conjunctival mucous membrane was hanging in oedematous folds. Dr.

Edward Ryan said that unless the exophthalmos could be relieved by partial thyroidectomy she must lose her eyes. I operated with a pulse so rapid that at times it could not be counted. Her pulse is now in the eighties, but one eye has gone completely; and although the cornea is still transparent in the other, we are not yet sure what will happen. Then there are all the cases which have advanced from Class I to Class II, those in which the damage is irreparable; I think one cannot ignore evidence like that.

Then there is the question as to how much gland tissue should be removed. We know the immense physiological importance of the thyroid gland, and yet here we have it poisoning heart muscle, poisoning nerve tissue, causing exophthalmos and emaciation. We have to remove enough to cure the disease, and we must leave enough for physiological purposes, and all the judgment and experience which one has is called for. In young patients, and those not very bad, the larger lobe should be enough, with any mid-lobe or isthmus. In older people, and those in whom the disease is very bad, the removal of one lobe will practically not do any good at all; one lobe and half the other must be removed. If the gland has been big and active, even then the remaining portion may be too large. One has to remember that more can always be removed, but it cannot be put back again easily. One must remove enough, but one must never be hustled into removing too much in order to make a "complete job" at once. Although I now rarely have to operate more than once, it will occasionally happen that one has to remove some more to cure the patient completely, and in three cases I have operated three times. They were among my earlier cases, and only one lobe was removed at first; they were also among the earlier cases in which I was recognizing that part of the second lobe had to be removed, hence I was very frightened of removing too much. So later I removed a third portion. I am sure it was wiser to go slowly and safely in the way I did; it all had to be, in the way of finding out knowledge.

Anæsthesia.—Now as regards anæsthesia, with the exception of a very few cases in which open ether has been given by Dr. Harse or Dr. Davies, all my operations have been performed under local anæsthesia. I know that in many instances general anæsthesia may be quite safely given, but in a great many instances it cannot. All the causes of death in this operation are not known, chief among them are crushing and handling of gland tissue, slow operating, inexperience. General

anæsthesia alone is not the chief cause of death, but I like operating under local anæsthesia; the patients are safe, the distress is negligible, the recurrent laryngeal nerve may be guarded, post-operative vomiting does not occur, pints of fluid may be given by the mouth. And the moment the operation is over the patient is happy enough to smile, and free from the unpleasant sequelæ of general anæsthesia. General anæsthesia could not be given in cases in Class II, and scarcely in the worst cases of Class I. Almost always the upper pole, or a pear-shaped protuberance from the posterior edge of the middle of the lobe, wraps itself tightly around the trachea, almost behind the trachea. In these cases there is a little "drag," but I submit that that protuberance is more safely shelled out and off the trachea by gentle manipulation under local anæsthesia. In many instances, with nervous patients I have placed the apparatus for general anæsthesia on a shelf in the room, and told the patient that she might have it on demand. I have never had to change, and have long ceased to carry the apparatus. Local anæsthesia means using 7 oz. of 2 per 1,000 novocain, and well infiltrating all the front of the neck.

As regards exophthalmos, the reports that occur in the literature differ very widely. I find that if one lobe and a portion of the other be removed the eye corresponding to the complete removal recedes much more than the other. If sufficient gland substance has been removed to cure the general condition, the eyes, even if they have been very prominent, almost always recede in a longer or shorter time. One lady whose eyes were very proptosed, and looked quite uncanny, became normal in appearance within a fortnight of operation. Another who had two operations took ten months. I have mentioned the lady whose eyes were so proptosed that one was [destroyed, the other receded after operation but not completely; and a few always have a little proptosis remaining.

About the parathyroids, I have not evidence from which to speak. In 380 operations I have never seen evidence of tetany. I certainly strip back the posterior capsule as carefully as I can, but I never do the intracapsular ligation of vessels, as insisted on by some American writers. If they are as readily damaged as the literature would show, I must have damaged them many scores of times. At present I have to suspend judgment.

I think, again (this is only opinion), that if the removal is rapid and gentle, removal of one lobe and a half is possibly less dangerous than

removal of one lobe alone, for the following reasons: removal of one lobe, I believe, causes reflex dilatation of the vessels of the other lobe, with increased activity of the gland. The remaining lobe being tightly encapsuled by its capsule, must pour the results of its increased activity into the lymph and blood vascular systems, with consequent poisoning. If all of one lobe and half the second be removed *without crushing*, the clean-cut surface of the second lobe allows free escape for the thyroid secretion and lymph, which is led to the exterior by an efficient drainage tube. This supposition would certainly not hold good with slow operating or rough handling of the gland. The operation must frequently result in failure if only one lobe is removed, the other lobe being at the same time large and vascular. Removal of one lobe may not do a patient any good at all, and it is because so much thyroid tissue is left behind that the operation is so frequently spoken of as not being successful.

The fear that these patients may become myxœdematous has been expressed to me frequently. The operation is being performed extensively the world over now, and many critical eyes are watching results. I think no case of myxœdema following operation would escape observation. On the other hand, I think the greater fear is that, without operation, many cases will pass from Class I to Class II, or else come too late for surgical interference.

In Osler's "System of Medicine" the statement is made that the disease is one in which "few recover and some die." Against that one can say that one has seen individuals so miserably wretched that life was burdensome, become in one week absolutely calm, lose all tremor, and in a few weeks able to enjoy life actively; others who though not quite so bad are unable to do work except with constant distress, become in a few weeks able to undertake their duties with comfort. They play tennis, they ride, they dance; one man builds coaches, one, who was very ill, has returned to his work as a blacksmith. If, rarely, there is one in whom, through not quite enough tissue being removed, the heart beats still too rapidly, one feels that it is better to err on the safe side, and it does not detract from the result in scores of patients who are leading vigorous lives.

DISCUSSION.

SIR VICTOR HORSLEY said that he could add little to what he had contributed to the discussion at a meeting of the Hunterian Society held last year. As regards the pathology of Graves's disease, he did not entirely agree with Dr. Dunhill's classification into four classes of cases. He (Sir Victor Horsley) recognized three forms: (1) True exophthalmic goitre with watery secretion; (2) parenchymatous goitre with exophthalmic symptoms; (3) an extremely rare form in which the gland was wholly diseased, and in which he advised total removal and grafting of normal gland beneath the peritoneum. He agreed with Dr. Dunhill's view that the danger of operation was *nil*; that was his (Sir Victor Horsley's) own experience. He had had one death only, and that many years ago. It was true, however, that he had refused to operate upon three cases, and so possibly avoided a higher mortality. The high death-rates published must depend upon an incorrect estimation of the condition before operation. It was only fatal in *dernier ressort* cases. With regard to the method of operation, he had given up that by ligature of the arteries and did not consider that it cured like removal of the lateral lobe and isthmus. It was true that certain symptoms persisted afterwards, such as hurried heart action on exertion and a degree of exophthalmos, but the patients returned to work, and that was the test of surgical treatment. All his cases had been subjected for many months to medical treatment. He thought three months was long enough to wait before resorting to surgical measures. No medical treatment would cure parenchymatous goitre with exophthalmic symptoms in an adult. True exophthalmic goitre, however, often got well with faradism and rest cure treatment. With regard to the means of producing anæsthesia, he had operated upon severe cases and always under general anæsthesia, and had seen no reason to depart from that method. He considered that the method of anæsthesia had no bearing on the prognosis. He admitted that too often an excess of anæsthetic was given. He had seen no deaths from the general anæsthetic and did not think that it should be held responsible for deaths in these cases.

Dr. GEORGE MURRAY: I have been asked on this occasion briefly to consider the general principles of the treatment of exophthalmic goitre, as it is important that these should be clearly stated as a basis for the

discussion on the best means of carrying them into practice by either medical or surgical methods.

It is now generally agreed that the symptoms of Graves's disease are due to a thyroïdal auto-intoxication. In Graves's disease the secretory epithelium of the thyroid gland is superabundant, changed in type, and over-active. Whether the secretion which results from this state of affairs is of the same strength and composition as that which is produced in health does not materially affect the problem we are asked to consider on this occasion, as the general symptoms of the disorder are brought about by the circulation in the blood of a large excess of this product, whatever its actual composition may be.

We do not, as yet, know the actual exciting cause of the special proliferative changes which are found in the thyroid gland in exophthalmic goitre. We are aware that the disease may arise under certain predisposing conditions, but these vary in different cases and in many may be wanting altogether. When we are in possession of this information so that we can induce the disease at will in lower animals, the problem of the prevention and treatment of this malady will be greatly simplified. In the present state of our knowledge the objects we have in view in the treatment of Graves's disease are either to remove the source of the auto-intoxication or to counteract its ill-effects. The principles of treatment are therefore comparable to those which guide us in the treatment of a disease which is due to a local microbic infection, giving rise to a general toxæmia, but more difficult to carry into practice.

In some cases we know that either as the result of treatment or in the natural course of the disease, the hyper-activity of the thyroid gland gradually diminishes, the symptoms subside, and the patient recovers more or less completely. According to my own experience this may take any period from nine months up to seven or more years, from the commencement of the disease. In some chronic cases a certain amount of tolerance gradually becomes established, so that the patient is hardly aware that the disease is still present. Recovery in these cases is the result of an involution of the enlarged gland, due to an atrophy of the redundant epithelium. This atrophy may be either primary in origin or secondary to the development of a gradual fibrosis of the gland, which may proceed to partial or even total destruction of the glandular epithelium, as in a case I have recently seen in which the symptoms of Graves's disease were replaced within a few months by those of

myxœdema. We are greatly in need of more exact information as to the conditions under which those involutionary changes take place. If we possessed this knowledge, we should be in a better position to bring this natural process of cure into operation.

We shall now briefly review the methods which may be adopted to reduce the morbid activity of the thyroid gland to a normal level, or to counteract its ill-effects, reserving the consideration of surgical measures to the last.

General treatment by means of mental and bodily rest, combined with a liberal diet—of which milk forms a large proportion—tends to diminish thyroidal activity. Excess of proteid food should be avoided, as Dr. Chalmers Watson's experiments show that the structure of the thyroid gland may be modified by diet. The work of Ehrlich and Wassermann opens up the possibility of efficient remedies being obtained in the future which may have a direct and selective action on the hypertrophied gland. It is not unlikely that arsenic and belladonna, which are of proved utility, act in this way and tend to depress the activity of the secretory cells, just as iodine on the other hand exalts it and aggravates the symptoms. With the same object in view attempts have been made to prepare a specific cytolytic serum which would induce destructive changes in the epithelium of the gland without injury to cells in other parts of the body. Unfortunately such preparations are not really specific in action, and if used in adequate amounts they produce degenerative changes in other organs as well, and consequently may do more harm than good. X-rays have been employed in order to diminish the gland. In one of my cases at the Manchester Royal Infirmary eleven doses of X-rays were given between November 28, 1911, and January 5, 1912, by Mr. Barclay. On January 9 the right lobe of the gland was removed, because one night the patient had a severe attack of dyspnœa with loss of consciousness for ten minutes. Microscopical examination of sections prepared by Dr. Mair from the portion removed shows there is a diffuse interalveolar fibrosis, which, in places at any rate, appears to be of recent origin, and to be the result of the action of the X-rays. At the time of the operation Mr. Burgess found the capsule of the gland was unusually adherent to the trachea and surrounding parts. These adhesions were probably also a result of the use of X-rays. Although in this case no beneficial result was obtained by X-ray treatment, the microscopical changes suggest that a more prolonged course of treatment might in time bring about the desired result.

The application of a mild faradic current to the goitre for two or three hours each day possibly acts directly on the activity of the gland, as in many cases it is a useful mode of treatment.

We may endeavour to counteract the ill-effects produced by the excess of secretion in the blood-stream. For this purpose the milk, dried blood, and blood serum of thyroidless animals, especially of sheep and goats, may be employed, on the supposition that the products contain some substance which acts as an antidote and neutralizes the action of the excess of thyroid secretion in the blood. In many cases we have to resort to purely symptomatic treatment under special circumstances so as to deal with the special crises which arise from time to time in Graves's disease, when special measures may be applied to relieve cardiac, intestinal, bronchial, cutaneous or nervous crises giving rise respectively to severe palpitation, diarrhoea, bronchorrhoea, sweating, and the like.

Finally, I will briefly mention some points in connexion with surgical treatment. As the first object we have in view is to reduce the hyperactivity of the thyroid gland, it naturally occurred to many that this could be most successfully achieved by surgical methods. This view appealed rather strongly to me when the pathology of Graves's disease first became understood, but very quickly the hazardous nature of the proceeding became apparent. The first three of my cases in which one lobe of the thyroid gland was excised, in each case by a different surgeon, all died almost immediately after the operation. After this experience I was very reluctant for long to advise any patient to undergo operation, and consequently my personal experience of surgical treatment is limited.

Two methods of surgical treatment are chiefly employed at the present time: ligature of one or more of the thyroid arteries and partial thyroidectomy. In referring to the notes of 300 of the cases which I have seen, 276 of which were women and 24 men, I find that as far as I know only ten have been operated on. In one case both superior thyroid arteries were ligatured, and in nine partial thyroidectomy was performed. In the first three cases, which were all in women, death occurred shortly after the operation. The other seven recovered from the operation, so that of the cases I have seen in which an operation was performed the mortality has been 30 per cent. Two of these seven were men and five were women. In one man who had suffered for nine years from severe Graves's disease both superior thyroid arteries

were ligatured by Mr. R. Morison in June, 1907, under general anaesthesia, four and a half years ago. Marked improvement has taken place, so that he can now cycle to and from his place of business and do an ordinary day's work, but he is not cured. In the second man, whom I saw in 1909, just before he started for Canada, partial thyroidectomy was performed by Mr. Roberts, of Toronto, in May, 1911, and when I saw him the following September he was quite well and completely cured of the Graves's disease. Of the five cases in women, in one, that of a single woman, aged 32, in whom there had been a goitre for twelve years, with more recent development of secondary Graves's disease, the right lobe was excised by Mr. W. G. Richardson in June, 1907, because she complained of much pain in it and was anxious to have it removed. The only anaesthetic used was chloroform, given through the Harcourt inhaler. At the time the heart was considerably dilated, and the pulse 144. She recovered, and her medical adviser, Dr. A. Smith, informs me that she is now quite well. In another case, that of a girl, aged 15 when I saw her, the operation was performed by Sir Victor Horsley, and when last I heard of the patient marked improvement had taken place. In the case of a woman, aged 32, under my care at the Manchester Royal Infirmary, Mr. Thorburn, on August 16, 1910, removed the right lobe of the gland under local anaesthesia. Before the operation the pulse-rate was 130; it is now 76, and she has improved considerably in other respects, but there is still well-marked exophthalmos, some general nervousness, and tremor of the hands. The left lobe is still moderately enlarged, so that she is not cured. In a recent case in the Manchester Royal Infirmary, already referred to, Mr. Burgess removed the right lobe on January 9 from a girl, aged 18, with severe Graves's disease, because after eleven doses of X-rays she had an alarming attack of nocturnal dyspnoea with loss of consciousness lasting for ten minutes. Ether was given by the open method. Before the operation the pulse varied from 204 to 120. She recovered from the operation, and is now steadily improving, the pulse varying from 120 to 92. In another case Mr. Burgess has also this month removed the left lobe, isthmus and lower part of right lobe on account of stridor. Thus in six of my cases an operation has been done in order to relieve or cure the Graves's disease, and three of them died. In the remaining four the operation was primarily carried out for the relief of pain or dyspnoea. Of the seven survivors, two are cured, four have improved, and one has just recovered from the operation.

In conclusion, I would advocate operation in all cases where there is distinct stridor from compression of the trachea or persistent pain in the goitre. In cases of a mild type I do not consider an operation is necessary. In very severe cases with marked cardiac failure the risk is too great. In a certain number of cases of moderate severity in which no adequate improvement has resulted from medical treatment fully tried for twelve months, a partial thyroidectomy or ligature of the superior thyroid arteries may be advised. The remarkably small mortality from the operation obtained by Sir V. Horsley, Dr. Dunhill, Professor Kocher and others clearly indicate that the grave dangers which formerly made physicians unwilling to advise operation have now been considerably reduced, so that operation can be recommended in a larger number of cases than previously appeared to be advisable. The chief points upon which we hope to obtain further information by this discussion are the exact indications for operation, the average risk, and the results. In considering the latter and in comparing them with those obtained by other methods of treatment, I would emphasize the fact that the prognosis usually given in text-books is too pessimistic, as a very considerable number of cases do either completely or partially recover without operation.

MR. C. LEEDHAM-GREEN: Dr. Dunhill's paper offers a great number of points for discussion. I wish to confine myself to a consideration of exophthalmic goitre. The operative treatment of simple goitre, thanks to the work of Kocher and others, is so eminently satisfactory and so free from danger that, for the majority of cases, it is quite immaterial whether a general or local anæsthetic is employed. When we, however, turn to consider exophthalmic goitre we are confronted with the knowledge that in England any form of operative treatment is still looked upon askance. The physicians, on the one hand, have not accepted the claims which have been put forward by Continental surgeons and, on the other hand, few of our countrymen have had much experience in the operative treatment of these cases. I, like most of my countrymen up to the present, have operated on far too few (thirty-five cases) to enable me to make any dogmatic statement. And I should not venture to speak to-night had I not had special opportunities of supplementing my own experience by observing the results obtained in some of the large clinics abroad.

As Dr. Dunhill says, the first question to be answered is *whether*

surgical interference is justifiable. To answer this in the affirmative we must be able to show that our results are not only better than those obtained by conservative measures, but also that the danger of an operation is not excessive.

Let me first take the question of *the mortality of the operative treatment of exophthalmic goitre.* When this subject was discussed at the annual meeting of the British Medical Association in 1910, a very gloomy view was taken of the danger of the operation. The discussion opened with an unduly pessimistic note, which it never lost. Everyone who had had, or had heard of, a death after the operation, seemed, for once in a while, pleased to publish it. At present it is not easy to state what is the mortality of the operation; for, not only is there still a great difference of opinion as to what are the indications calling for operation, but also what even is to be classed as exophthalmic goitre.

At the German Surgical Congress last Easter six surgeons, including such experts as Theodor Kocher, von Eiselsberg, Garré, and Hildebrand, quoted their mortality, which varied as much as from 3 to 17·3 per cent., or, taking the total of cases (883), gave an *average mortality* of a little over 5 per cent.—an operative rate which can hardly be described as prohibitive, though, of course, very much higher than that of ordinary goitre.

Do the results of the operation warrant such a risk? In order to answer this we must compare them with the results obtained by conservatively treated cases, and also inquire into their permanency.

What is the mortality of exophthalmic cases treated by conservative measures? It is a question well worthy of study, for at present the data on which to base an opinion are few; but, taking the average of many hundreds of published cases, it works out at about 15 per cent. I am quite aware that this mortality is based upon figures taken from large clinical hospitals where the patients are poor and unable to afford the time requisite for the constitutional treatment; and I merely bring them forward in contrast to the statement, which is not infrequently made by English physicians, that this disease does not run a fatal course.

But, looking aside from the question of mortality, *how do the methods compare as regards restoration to health?* That the immediate result from operation is generally good—strikingly good—I think all who have seen much of this work will agree. It is a common experience to find that a patient who, prior to the operation, had had for months a pulse-

rate of over 160, within a few days of the operation has one that has sunk to 60 or 70, and, with the slowing and steadying of the heart, all the distressing nervous symptoms have vanished. What other treatment is capable of this? It is true all cases do not respond so well or so quickly; time will not allow me to discuss these unfavourable forms.

But are these results permanent, or do the symptoms generally return after a lapse of time? This is a more difficult question to answer, for, though exophthalmic goitre has been operated upon since 1880, it is only during the last decade that it has been done systematically. And, further, it must be remembered that the present operation is much more thorough than it was, even a few years ago.

Garré, at the Berlin Congress of last year, out of 65 cases, owned to 10 or 15 per cent. failures, in spite of thorough operative removal of the gland tissue (in 20 per cent. of the cases the exophthalmos was unaffected, in 10 per cent. the tachycardia was still present). Von Eiselsberg (71 cases) reported 23 completely healed (with the exception of the exophthalmos); 8 improved (some tachycardia present); 2 unrelieved. Küttner collected 85 marked cases of exophthalmic goitre which had been treated during recent years in the Breslau Klinik. Of these 85 cases, 21 were treated conservatively (not operated on): 2 of these died in the Klinik, 3 died later of heart trouble; of the remaining 16 cases, 9 could be traced. None of them were cured, only one moderately severe case felt better. All the others continued to suffer as before, or were worse, and unable to work. Of the 63 cases operated upon, 11 died; of the remaining 52 cases, 37 were traced and 31 personally examined. Of these 33·2 per cent. were completely cured, showing no sign of the disease; 36 per cent. showed marked improvement and were at work; 16·6 were able to work, but still showed some definite Graves's symptom; in 13·8 per cent. no permanent benefit accrued. Or, to put it briefly, *of the medicinally treated*, 35·7 per cent. died of the disease, none was cured, and only one able to work. Of those *operated upon*, 17·3 per cent. died; 13·8 per cent. unrelieved; 86·2 per cent. cured, or sufficiently so as to be able to work.

My own cases, just over 30 in number, are too few and too recent to be worthy of much consideration, the bulk of them having been done during the last five years. I have to own to three deaths: one from acute pneumonia, one from heart failure, and one some weeks after the operation, when the wound was completely healed, from an acute exacerbation of a slumbering phthisis. Of the remainder, all derived

unmistakable benefit from the operation; two have relapsed, the remaining portion of the thyroid having hypertrophied, and calling for a second operation. Of the other cases all are at work, several of them strenuously so. The mortality of my cases is high and might easily have been kept down by refusing to operate upon the gravely debilitated cases. But, personally, I do not think it right to refuse to operate upon these severe cases because of the extreme danger to the patient. If I have had the misfortune to lose some, on the other hand I have had the satisfaction of remarkable success among patients who were dying, and had been refused operation on account of their extreme condition, but are now able to work and earn their living.

What are the indications for operation? Up to the present time it must be owned that the only indication for operation recognized in this country is as a last resort where every other treatment has failed and the patient is rapidly drifting away. That such patients are ill-fitted both to undergo an operation and to offer a fair test both as to the danger and efficacy of the operation, must, I think, be conceded by all. If the operation is to have a reasonable chance of curing the patient, then it must be resorted to before the vascular and nervous systems are shattered by the prolonged ill-effects of the morbid thyroid secretion. I do not for a moment suggest that every slight case of exophthalmic goitre should be subjected to an operation, but I do urge that, as soon as the effects of rest and medicinal treatment have been shown to be of no avail, valuable time shall not be wasted before the question of resection is considered. I maintain that the benefit, both immediate and remote, of the operative treatment has now been demonstrated and that the only objection that can be urged against it is its relatively high mortality. This, however, is rapidly falling and will no doubt continue to do so as surgeons improve the technique, and more especially as patients are submitted to the treatment at an earlier stage.

To what extent is interference desirable? Undoubtedly the tendency is to operate more radically than was the custom even a few years ago, and the results seem to justify it. Certainly in my own cases my best results have been obtained where I have removed the most. It is, however, often difficult to say what is the best procedure to adopt when dealing with a gravely affected case. Ought we to content ourselves with the preliminary ligature of one of the superior arteries under local anæsthesia, as advocated by Professor Kocher, leaving the resection

of the gland to a subsequent operation, or is it better at once to resect the gland? Against the preliminary ligature of one of the superior vessels it may be urged that the risk of the operation seems unduly great for the benefit it confers. Even in Professor Kocher's hands it accounted for five out of his total seventeen deaths.

Anæsthesia.—In patients whose resistance is so notoriously low the question of the anæsthesia is of considerable importance. We have so little margin of safety to work on that we cannot afford to neglect the smallest point in the patient's favour. There can be no question that from a theoretical point of view local anæsthesia has much to recommend it. The great danger of the operation lies in the liability to subsequent pneumonia and cardiac failure, and few will question that a general anæsthetic is more likely to favour the onset of these complications than is a local anæsthetic. But, on the other hand, it must be remembered that if these cases are poor subjects for inhalation anæsthesia, they are also far from being ideal for the local form. They are highly nervous, restless and unreasonable, and, unless the surgeon is both conversant with the production of local anæsthesia and accustomed to operate under its influence, he will do better to work under general anæsthesia.

Personally I prefer local anæsthesia, which I use very largely as a routine anæsthetic in general surgical work. But in either case I administer a preliminary dose of scopolamine and morphia.

Mr. J. LYNN THOMAS, C.B., said Dr. Dunhill's paper was to him a source of pleasant surprise and encouragement, for up to the time of reading the paper he had regarded partial thyroidectomy for Graves's disease as one of the most anxious operations he undertook, because of the invariably serious disturbance of the heart which soon followed it, notwithstanding the fact that either a local or a general anæsthetic might be used. Just before the discussion at the Medical Society of London in April, 1907, he had the privilege of visiting the clinic of the Mayo Brothers, and there he saw open ether anæsthesia, and from that time he had invariably used novocain 1 per cent., copying Professor Kocher, whose work he had seen many times. After experience with open ether combined with oxygen, he was of the same opinion as Sir Victor Horsley, that the anæsthetic was but a small factor in the determination of the success of the operation. He had had altogether four deaths in connexion with the treatment of Graves's disease. He always

had patients under observation for weeks, sometimes months, before operating upon them, and he never operated upon a patient unless he or she had complete confidence in him; he showed them the operating room, and trained them to get used to the ether. One of his patients who had confidence in him came to the operating theatre; he left her to get ready for an operation, and when he came back she suddenly died, probably of acute emotional disturbance. Another case died from pneumonia after he had removed the goitre under novocain—fortunately for the reputation of ether. Another case died after ether from pneumonia; he had used there open ether with oxygen. In Wales most of the cases of exophthalmic goitre which he had come across came from near the sea; he had not had any cases from the mountain top. Some years ago he made inquiries about the distribution of goitres in Wales, and was much surprised that along the peninsula in Carnarvonshire one medical man had ten cases of exophthalmic goitre under his care at that particular time, and not a single case of ordinary simple goitre. As a result of that experience, all the cases which he now operated upon were sent inland to the top of the mountain. He had a remarkable experience last month showing the effect of emotion upon patients after an operation. He operated upon two cases at the Cardiff Infirmary within a week; one was a bad case of exophthalmic goitre, in which the pulse-rate could not be brought lower than 100 by months of careful treatment. There was a very big goitre indeed, weighing nearly 3 lb, and the exophthalmos he operated upon five days before. On the eighth day the parenchymatous case was allowed to go home. The pulse-rate of the case of exophthalmic goitre had dropped from 180 to the nineties, and when she found she would not be permitted to go home the same day her pulse jumped up to over 140. That illustrated the great importance of keeping an eye on the after-treatment of these cases. He passed round a photograph of an ordinary goitre in which the anæsthesia was ether with oxygen. It was the worst case of goitre he had attacked, and there was much respiratory trouble. She had been purple in the face for many years, the veins in the face stood out prominently, and the goitre extended down into both posterior triangles, and the veins of the upper extremities were always congested. He thought that confirmed what Sir Victor Horsley said regarding the anæsthetic, that it was really a question of having an expert anæsthetist.

Dr. HALE WHITE remarked that what he had to say had reference to cases of exophthalmic goitre which came into Guy's Hospital between the years 1888 and 1907—twenty years—and all the cases seen by himself in private. Full details of each case and the statistical results of treatment and prognosis would be found in a paper entitled "The Outlook of Sufferers from Exophthalmic Goitre."¹ Many of the patients could not be traced. The total number, if they could all have been traced, was over 200. He had excluded from the first consideration those which had been operated upon, because his object was to discover what was the course of the disease in the patients who were not operated upon; one must first learn that before being able to know whether operation was useful or not. He could trace 49 patients among the hospital ones, and 53 whom he had seen outside. The next step seemed to be to determine what was the mortality of people suffering from exophthalmic goitre as contrasted with the mortality of healthy people of the same age. This was an actuarial question, but fortunately he was able to get Mr. Thistleton to answer it for him. Among the hospital patients, according to the experience of healthy females based upon the table of twenty British offices, the expected deaths would be five. The actual deaths among these hospital patients numbered eight. Taking only the cases between 30 and 45 years of age, there were five deaths, and there should have been three. Among private cases there were seven actual deaths, the expected number was three. These figures suggested that if more cases could be got they might be able to prove, beyond all cavil, that as the total number of deaths of private and hospital cases not operated on was fifteen, and the expected deaths among similar healthy people would be eight, the mortality among sufferers from exophthalmic goitre was about twice that among the general population for the same age and the same time. But it must be remembered that one was dealing with people at an age at which the expected deaths were few, and therefore fifteen was not an excessive mortality. But those figures must not be transferred to exophthalmic goitre at large, because these cases were in people who were ill enough to come into hospital, or among private patients, to seek a second opinion. Therefore, there were no mild cases from which one might infer that the expectation of life among those with exophthalmic

¹ *Quart. Journ. Med.*, Oxford, 1910, iv, pp. 89-99.

goitre, not operated upon, was better than the figures here given. But he admitted those figures did not include people who died in the hospital. But for those interested in the problem of whether to operate, the patients who died in the hospital did not matter, for all those who died in the hospital were so bad that, as Sir Victor Horsley said, they should not be operated upon. The fatal cases were of interest as showing the cause of death of sufferers from this disease. Of the 18 patients not operated upon, who died in hospital, 11 died from diarrhoea and vomiting. In 6 there were nervous symptoms, delirium and coma, and 2 had melancholia, 1 had mania, 1 had mental disease, 1 endocarditis, 2 rheumatic fever, 2 pneumonia and broncho-pneumonia, and 1 died of diabetic coma. Of the cases seen outside the hospital the deaths were much the same, except that 2 died of diabetic coma. The first cases he wished to refer to were in those whom he succeeded in tracing, who were not operated upon, and who did not die in the hospital. There were 40 of them, and he had grouped them into those who, by their replies to his letter or as the result of his seeing them, he could say had done well. Of the 40, 26 did well; 12 described themselves as having been moderately well or better; and 2 were not. Those who did well did very well. To take one or two of these at random from the list, No. 4 was a bad case, which was in the hospital twenty years ago. The patient had worked hard for eighteen years, had married and had three children, and was now a widow. Another was in the hospital sixteen years ago, felt well, and had not had a doctor for twelve years. Another was in the hospital five and a quarter years ago, and had been well ever since she left the hospital. She went into service for four years, then married, had four children, and never needed a doctor, although she said she paid into a club. He had been unduly rigorous in ruling out cases and putting them into the second group where they had only done moderately well; yet many of the second group might with equal justice have been put into the group which had done well. For example, he had put one into the middle group because she said her health was fairly good, but she had been able to take a situation, then marry and have two children. Of the patients seen outside, there were 47 to be considered: 35 reported themselves as having been well, 9 moderately well, while 3 had not been well. One of those who had done well would interest the meeting. One of the speakers referred to the possibility of the remainder of the gland hypertrophying after one

lobe was removed. That was very rare, but this case showed it might be a danger. Seven years before he saw the patient she had had one lobe of the thyroid removed for the disease, and got better for a time. Then the disease returned, and when he saw her she had most of the symptoms of exophthalmic goitre, including enormous hypertrophy of the remaining lobe, present in extreme degree; but after prolonged and continuous rest she got well, and could now walk to business and do a day's hard work. Her sister had the disease severely at the same time that the patient underwent operation, but she was not operated upon, and she got well. Another case of interest was that of a woman who had had an exophthalmic goitre with fibroid of the uterus. The fibroid shrank, and so did the thyroid. She got well except for very slight exophthalmos, and when he saw her she was an old lady, and was suffering from acute pneumonia, from which she recovered, in spite of her previous exophthalmic goitre. Another case showing how well such patients did, was that of a woman he saw fourteen years ago, who had glycosuria with her exophthalmic goitre. That disappeared in two years, and had not returned since. The total number of cases which he could bring forward was 87. Of those, 61 on their own showing fell into the category of having done well, 21 did moderately well, and 5 were no better. Of the cases outside the hospital, the severe cases did better than those among hospital patients. For example, of the 35 cases which had done well outside the hospital, 8 he grouped, when he saw them, into the severe class; whereas, of the hospital severe cases, there was only one.

With regard to the operations, he had but little to say. Eleven of his series were operated upon; 4 of them died as the result of the operation, but the operations were done some time ago, and very likely patients with that severity of illness would not be operated upon nowadays. But only one of the patients who did not die reported herself as perfectly well when written to; the others said they were much better but were not completely cured. If one excluded the patients who were so ill that they died while in hospital and therefore were unsuitable subjects for operation, and followed for some years the patients discharged from hospital and those seen in private practice, the actual deaths of the sufferers from exophthalmic goitre ill enough to go into hospital numbered 15, as against 8 amongst healthy females. As the cases selected for operation were chosen chiefly from mild cases and a few died from the operation, it scarcely seemed likely that operations on

the thyroid could greatly diminish the deaths that might be expected if the patients had not been operated upon. It seemed to him that in the future, when the operation had been made safe, the object of the operation would be not to prevent the patient dying from the disease—for the disease, as had been shown, did not kill many, in proof of which he urged that it was uncommon in the post-mortem room, and usually got well, for it was rare among old people—but because after operation the patient would get well more quickly than by medical means. This could only be shown by a large number of cases, in regard to which there was information as to how completely they were cured. Many expressions had been heard at the meeting to the effect that operation did not completely cure. Further, it would have to be shown that the patients were then better able to do their work than those who had not been operated upon, and able to get back to their work more quickly. And lastly, the ultimate test must be actuarial; one must know what was the expectancy of life of a woman who had part of her thyroid removed; and this could not be settled for some years. When it was settled it must be upon actuarial computation.

(The Discussion was adjourned until February 27.)

Surgical Section.

JOINT MEETING WITH THE MEDICAL SECTION AND SECTION OF ANÆSTHETICS.

February 27, 1912.

Dr. FREDERICK TAYLOR, President of the Medical Section, in the Chair.

Discussion on Partial Thyroidectomy under Local Anæsthesia, with Special Reference to Exophthalmic Goitre.¹

Dr. HECTOR MACKENZIE said that in opening this second day's debate on Dr. Dunhill's paper—a paper which was both remarkable and important—he wished first to make a few observations on the paper itself; next to offer a few remarks on his own experience of the disease; and finally to attempt to arrive at a right conclusion as to the kind of treatment which was best and safest for the patients who came under care with the condition. He desired to remind the Section of the remarkable and dramatic story with which Dr. Dunhill opened his paper. The author said he had been treating a number of patients with the milk of thyroidectomized goats, in the outpatient department of his hospital. He (Dr. Mackenzie) did not think it practical in the outpatient department of a large London hospital to carry out such a method of treatment on any large scale. Goats took some time to prepare for this purpose, and the whole of the milk of one goat was scarcely sufficient for one patient, so that the limit to the number of patients who could be treated in this way must soon have been reached. In Dr. Dunhill's outpatient department a woman arrived who was very ill, and it would seem there was not available a supply of the special milk. She asked for something to be done to relieve her, and he talked over with her the possibility of effecting some improvement

¹ Second meeting (adjourned from February 13).

by operation. She decided to have the operation done, and the operation was successfully performed. Then after the operation those patients who had been attending the outpatient department went up to the ward to see her, and were so delighted with the improvement which had taken place in her condition that one after another they requested to be operated upon themselves. And one found from the paper that in a few years its author had operated upon no fewer than 230 cases of exophthalmic goitre. Dr. Dunhill was to be congratulated warmly on his results from the surgical point of view, especially in having had such a low mortality amounting to only four cases. He thought all at that meeting would have been glad if Dr. Dunhill had supplied more details about the cases, as to their condition both before and after operation. Four types of the disease were mentioned, which need only be briefly referred to. The author did not say how many of his 230 cases belonged to the respective classes; but that was a very important matter. The first class were those with the classical symptoms of exophthalmic goitre. The second class comprised those in which there was cardiac failure, and probably cases of goitre with organic heart disease and failing compensation. In the third class there was little or no enlargement of the thyroid gland. In the last class there was goitre with one or other of the symptoms which one met with in cases of exophthalmic goitre. It was the lack of details which made it difficult for one to judge of Dr. Dunhill's results. It was difficult to tell how many of the 230 cases could be accepted as genuine cases of exophthalmic goitre.

The author said that with regard to cases in the first class, of frank complete exophthalmic goitre, the response to operative treatment was very prompt and the cure complete, if organic heart disease was not present and if sufficient gland were removed. It was always open to the surgeon to say, if the case did not turn out successfully, that organic heart disease was the cause of failure, or else that he had not removed sufficient of the gland. Dr. Dunhill said that in this class of case, provided local anæsthesia and expert operating were employed, the danger was *nil*. Dr. Dunhill said he himself had made use of general anæsthesia very little; therefore his experience with regard to the comparative merits of local and general anæsthesia did not help much. In London, on the other hand, local anæsthesia had hitherto been little used. He was much interested to hear Sir Victor Horsley say, at the last meeting, that he did not think there was any special advantage in local anæsthesia. It would be instructive to hear the views of Dr. Albert Kocher about local anæsthesia. He believed that while in Professor

Kocher's clinic local anæsthesia was the rule, in other parts of Switzerland general anæsthesia was more commonly employed. With regard to the comparative effects of medical and surgical treatment, it was of course very difficult to arrive at a proper conclusion. His own experience of cases treated on broad general medical lines was that about 25 per cent. made a good recovery. Another 25 per cent. were very much improved and, although not cured, the patients were in fair health and able to follow their occupations. Another 25 per cent. became more or less chronic invalids: the remaining 25 per cent. lost their lives from the disease itself after a longer or shorter illness. It was necessary to be sure that the results of surgical treatment were decidedly better than these, before recommending operation in a regular way to the patients.

He would like to say something concerning the experience of operation for the disease at St. Thomas's Hospital during the last few years. Up to the year 1908 comparatively few cases had been operated upon, though during all the time he had been connected with the Hospital such operations had been occasionally performed. While he was a student he remembered Mr. Sydney Jones dividing the isthmus in a case of exophthalmic goitre, and the patient dying very soon afterwards. At one time their experience of operative treatment was so bad that for a period the operation was rarely performed. But since 1908 operations had been more numerous. The total number of cases which had been operated upon in the last three or four years was 19, and of these 6 died. Of the 13 non-fatal cases there was marked improvement in 4, some improvement in 4, no change in 1, 2 relapsed and were readmitted, 2 were not followed up. A mortality of 6 in 19 was very heavy. There were two deaths shortly after operation, one death two days after, one death three days after, and one four weeks after; one death occurred a year after operation. So that four of the deaths were directly due to the operation, and two were not prevented by the operation, although not caused by it. One could not say that this experience was very encouraging. In some cases the superior thyroid vessels were ligatured, and in others thyroidectomy was done. Of the cases in which marked improvement occurred both superior thyroid vessels were tied in three, and in one of them in addition right hemi-thyroidectomy was done. Of the cases which improved, both superior thyroid vessels were tied in three, hemi-thyroidectomy was done in two, and both superior thyroids and right inferior thyroid were tied, and right hemi-thyroidectomy was done in another. During the last year nine of his own patients had been operated upon, in all the superior thyroid vessels

being ligatured. One of the patients died a fortnight after the operation. He did not think that death was due to the operation, but it was not prevented by it. The other patients all expressed themselves improved, but none of them were really cured. He believed Mr. Berry had collected statistics of the general results of operative treatment in the London hospitals, and it would be interesting to know how the experience of other hospitals compared with that at St. Thomas's.

If operative treatment could be made safe, and if its results proved to be superior to the results of skilful and judicious medical treatment, it would certainly be right to recommend it. A record of recovery from operation was not sufficient. The surgeons must produce their cures and show that the cure was permanent. Dr. Dunhill's cases had not been followed up for a sufficiently long time. How was one to tell that, although the symptoms of the disease had improved after operation, the patient would not relapse after a time? He had seen a patient who had been operated upon no fewer than three times; hemi-thyroidectomy twice in succession, and previous to that the superior thyroids were tied, and even now the patient was not very much improved. There was improvement for a time following the operation, and then relapse. For a long time he had been tending towards the adoption of operative treatment for these cases, but again and again his path had been beset with obstacles. There had been a relatively large proportion of deaths amongst the cases, and the results in those who had recovered from the operation had been, for the most part, disappointing. He believed there was a certain type of case in which it was always dangerous to operate, whether the anæsthesia was local or general—namely, the cases of what were called lymphatism, in which there was a large thymus and swelling of the lymphatic tissue. He thought operation should never be undertaken as a last resort. On the last occasion Mr. Leedham-Green said he was generally called upon to operate in cases in the last stage. His own belief was that a surgeon who operated on cases in the last stage was courting disaster. He had said before, and he said again, that were it not for the risk to life from thyroidectomy he would not hesitate to recommend it as the most rational and the most practical method of treating the disease. There appeared to be a good prospect of recovery under medical treatment in the milder forms of the disease, and there did not seem to be so much to be gained from operation in these cases as to justify one in encouraging the patient to run the risk of operation. In acute and severe cases he did not consider, in the light of present experience, that operation could be safely recommended.

Dr. ALBERT KOCHER (Berne): It was with great pleasure that I accepted the very kind invitation of the Secretary of your Society to take part in to-night's debate on "Exophthalmic Goitre." There are but few diseases on which more has been written in medical papers than Graves's disease. I am pleased to say that there is to-day nearly unanimity as to the pathogenesis of the disease being a functional trouble of the thyroid gland. The very different features, degrees, and course of the malady have, however, made it difficult up to the present to fix the exact functional change in the gland. Some pioneers, of whom I will only mention Sir Victor Horsley, Moebius, and Rehn, have, according to their own observations on different lines, described the disease as dysthyreosis or hyperthyreosis. The latter view, however, has gained ground very much by the results of surgical treatment, and my father, Theodor Kocher, who has been operating for thirty years on the thyroid gland in Graves's disease, is the main advocate of the theory of hyperthyroidism, basing his opinion on his extensive operative experience, of which he spoke at the meeting of the British Medical Association in 1910. The operations for Graves's disease in the surgical clinic at Berne up to date amount to 865, performed on 669 patients. With my father's kind permission I will speak of the whole of these cases, and not merely of my own, as we have observed and operated together on the great majority of these cases. As already mentioned by some of those who have spoken in the debate, it is difficult to class all the cases under one head. Allow me, therefore, to tell you in a few words how the different features of the disease have to be explained according to our present knowledge. (A) First, the different kinds of Graves's disease according to the condition of the thyroid gland itself (the following views are based on histological and chemical investigations on 200 glands of Graves's disease which will be published shortly in *Virchow's Archiv*). (1) The change in the thyroid gland in Graves's disease consists in the more rapid and more abundant absorption of the material stored in the gland-follicles. There is a considerable difference in the quantity and quality of the stored material present in the gland at the time of the outbreak of the disease. (2) There is a marked hypertrophy of the epithelium. Both these changes are connected with a hypervascularization of the gland. (3) If the disease is progressive all the stored-up material is sooner or later absorbed, according to its quantity and the rapidity of progress, and under further progression there is no more storing of material in the gland-follicles, but the proliferation of the epithelium is still progressive all through the gland, and degenerative changes of the epithelium can take place

together with formation and proliferation of lymphatic tissue. (B) The different kinds of Graves's disease as regards ætiology. In the outbreak of the disease we distinguish neurogenic causes which act through the vascular nerves, and toxic causes of chemical and infectious nature, acting through the blood. They can be acute or chronic, and they can also be combined.

I will not take up your time any longer with this complicated matter; you may judge from these few remarks that a large, if not *the* largest, part of the different features of the disease lies in the thyroid gland itself. I wish, however, to draw your attention to one more point. There are a great many cases, especially combined with nodular goitre, which present a few symptoms of Graves's disease, and only occasionally (especially after iodine treatment) show exacerbation or pronounced hyperthyreosis. Since surgical treatment of the disease has become more common a great many surgeons operate, and all *these cases* are apt to be registered as Graves's disease cured by operation. This is not quite right; we should always make the following distinction. (1) Cases with symptoms of hyperthyroidism presenting only occasionally pronounced hyperthyreosis, which, however, does not last and is not progressive, being usually the consequence of unlimited iodine treatment; (2) cases of steadily progressive, and (3) of periodically progressive Graves's disease. The first also come from sudden or very rapid and abundant absorption of the thyroid secretion stored in the gland-follicles (thyroid diarrhœa, as my father calls it), but when the cause of the outbreak has passed by the gland does not undergo further change—the disease is not progressive. In the cases of the second and third type this takes place, and after a certain time of duration degenerative changes may come on, not only in the thyroid gland itself, but also in other glands with internal secretion such as the adrenals, pancreas, thymus, spleen, liver, ovaries. In other organs also permanent changes are established, such as fatty degeneration of the muscles, especially of the heart muscle, also of the kidneys and of the liver. We can, therefore, before looking upon the results, presume that in progressive Graves's disease it is *most important at what period* of the disease we operate, whilst in simple hyperthyroidism we do not risk so much in postponing operation.

Amongst our list of 669 cases, 130 were of simple hyperthyroidism, mostly combined with nodular goitre of nearly every size, some presenting no extraordinary difficulty during the operation; some, however, partly or totally intrathoracic, and being combined with hyperthyreosis, very vascular and technically very difficult operations. These cases

have *all been entirely cured* of their symptoms of hyperthyreosis after the operation, with the exception of two, who died from post-operative pneumonia. In these cases we remove the cause of the disease with the goitre, and, more than that, we remove with the goitre the reservoir of the poison. Histological and chemical researches have shown that the goitre removed contains a large quantity of rather liquid colloid, in which an unusual amount of iodine is present. These cases are all suitable for operation if they are not complicated with other serious pathological changes in the lungs, heart, or kidneys. But it is advisable also to prepare these patients for operation by a short course of treatment, keeping away every toxic and nervous influence, because it is to be borne in mind for the operation itself that we have to deal with very sensitive people who are poisoned by toxins.

Five hundred and thirty-nine cases have been operated upon for steadily or periodically progressive Graves's disease. We are collecting the ultimate results, but with such a number they cannot be obtained as quickly as we should wish. We can at present give the ultimate results of 360 patients operated upon for progressive Graves's disease: 160 of these (45 per cent.) are radically cured, so that there is at the present time not one symptom of the disease left, and the function of the rest of the thyroid gland is normal. These cures last up to twenty-five years after the operation. The patients are leading a normal life, some working hard. Several lady patients have given birth to one or more healthy children since. Not all of these cases have been early ones; more than half were very severe and of long duration. The latter have been cured only after some time, during which several (up to five) operations have been performed on the same patient. The early cases have been cured a short time after *one* operation. One hundred and forty-nine cases (41 per cent.) show at the present moment, months or years after the operation, a few symptoms of the disease, but have been greatly benefited by the operation, inasmuch as patients of the working class, for instance, can earn their living without any difficulty. (a) Amongst these 149 cases there is first of all a considerable number in which a more extensive—that is to say, a second—operation would give complete recovery. Most of these patients, however, feel so well that they are unwilling to submit to any further operation. (b) In a small number of cases the only symptom still present is the exophthalmos, but they are not cases in which the bulb was most protruded before the operation, but cases in which the exophthalmos underwent no more change. They were sometimes combined with paresis of the bulbar muscles. I must mention here that among the 160 cases

radically cured, a very large number have had an extremely marked degree of exophthalmos; in one instance the bulb came quite out one day and had to be replaced. At the present time the eyes are normal. (c) A further group of cases show symptoms which had been present before the operation and were the result of the toxic influence on some of the organs, due to the severity and long duration of the disease, such as chronic myocarditis, chronic nephritis, and some degenerative trouble in other glands, such as diabetes, but all symptoms of Graves's disease have disappeared. (d) Some patients still show symptoms of functional trouble of the thyroid gland. There is no more progressive disease, but the part of the gland left does not seem able to adapt itself to the various demands. We sometimes find symptoms of hyperthyroidism and sometimes of hypothyreosis. The gland seems to be in a labile state. The cause of this is that the progressive changes in the gland, during the Graves's disease, had gone so far that it had lost its power of storing material in the gland-follicles, and the part of the gland left after operation was not able to regain this power.

However, all these 149 patients are cured of the great majority of the symptoms of Graves's disease and are able to lead a normal life. If we add this 41 per cent. to the 45 per cent. of complete cures, we can say that in 86 per cent. the ultimate result of operative treatment has been satisfactory. In 28 cases (8 per cent.) the ultimate result cannot be called a satisfactory one. (a) Amongst these we find cases in which the operative treatment has not been carried on so far as to obtain a satisfactory result. Some of these patients object to further operation, not having been benefited by the first one. In some, however, the disease has gone so far, and also the shock of the first operation—sometimes only ligation of one or two arteries—has been such that a more extensive operation seems too risky and is therefore abandoned. (b) The remaining cases of this group comprise those who have had recurrence of the disease. There are about 5 per cent. in all. In none, however, has the second attack been as severe as in the first instance—that is, before the operation. Amongst the cases registered as cured there is a number in which a second operation has cured the recurrent disease. Most of those also who show symptoms of recurrence might in a similar way be benefited by a further operation. But we have to bear in mind that partial removal (resection) of the remaining lobe of the gland in a recurrent case is extremely difficult, and therefore dangerous. It is true that in a few cases an excellent result has been obtained with it, but naturally the small part of the gland left has more difficulty in resuming its normal function. Twenty-two patients (6 per

cent.) have died since from other diseases. Only in a few instances does the former Graves's disease seem to be connected with the ultimate death. Five patients died very suddenly from what is called heart-stroke, after a fright or over-exertion, or in the course of an otherwise not dangerous (mostly infectious) disease. In all these cases Graves's disease had been of a very long standing, and had caused degenerative symptoms; however, after the operation the pure symptoms of the disease had disappeared. One patient died from diabetes. Whether this is in connexion with the degenerative influence of the severe Graves's disease on the pancreas remains doubtful.

This leads to the question "*What cases are suitable for operation?*" If we could operate in all cases within a short time, say half a year after the outbreak of the disease, and the sooner the more acute the outbreak is, I dare say *all* might be *cured* by operation. A short rest, with avoidance of all the things likely to cause progression of the disease, such as nervous strain and toxic influences, combined with more or less vegetarian diet and internal phosphorus preparations, is the proper preparation of these cases for operation. During this time a careful examination of the patient should be made, and this is *the chief point* to decide—whether an operation should be done or not in severe cases and of such long duration of the disease. Special attention must be paid to the heart, kidneys, liver, adrenals, pancreas, lymphatic organs (thymus, spleen, lymph-glands), and to the blood. A constantly irregular pulse, the persistence of a notable amount of albuminuria, very frequently fatty stools, distinct and constant, not only alimentary, glycosuria, low blood-pressure, marked status lymphaticus (especially the form without the otherwise characteristic lymphocytosis of the blood), a very high lymphocytosis of the blood, combined with very marked leucopenia, very slow coagulation of the blood—are conditions that *forbid* an operation unless they can be made to disappear under proper treatment during the time of preparation for the operation.

The operation itself consists either in the reduction of functional gland tissue by partial thyroidectomy or in the reduction of arterial supply by ligation of arteries. In early cases this will bring about a cure. In slightly enlarged, but very vascular glands, ligation of two or three arteries should be done; in larger glands hemi-thyroidectomy may be preferable. But one cannot fix any scheme, the most suitable operation for each case has to be decided upon individually. In severe cases of long duration the combined—that is to say, the consecutive—use of both operations is the method of choice. The ligation of the superior artery is best done from a small collar incision across the upper part

of the lateral lobe, between omohyoid and sternocleido-mastoid, the upper pole of the gland is set free and the artery tied or cut between two ligatures. The effect seems to be better if ligation of the thyroidal veins is omitted. In partial thyroidectomy the larger lobe with the middle part and pyramidal process should be removed. This is done with Kocher's symmetrical collar incision across the middle of both lobes. After dividing the straight muscles above the entrance of the nerve branches, the gland is carefully detached under exact hæmostasis of all the numerous accessory veins passing from the capsule to the gland. It is an advantage if the superior and inferior artery can be tied soon. Special care is to be taken at the back, where the recurrent laryngeal nerve and the upper parathyroid gland are adjacent. The best plan is to leave a sheath of gland tissue behind. Next, with regard to ligation of the inferior artery. The ligation of the inferior artery alone is as a rule a very difficult procedure, as it can only be done on the main branch, when the lateral lobe of the thyroid is lifted up. We do not therefore consider it the best method to be chosen, although it is the one lately chosen by most French surgeons. It has exceptionally to be done in cases where one lobe has been removed and the upper artery of the other tied. It is the same with the *partial removal or resection of the second lobe*. It is only exceptionally necessary and on account of the difficulty of hæmostasis not a safe procedure. The removal of one lobe and the partial removal of the other *in one operation* is a procedure which should not be undertaken. In early cases it is not necessary, in severe cases it is frequently the cause of death. We are sure that most of the cases lost after this operation could have been saved by consecutive operations performed at the necessary intervals.

All operation *can and should* be done under local anæsthesia. In early cases, where no symptoms of degeneration in the organs are present, general anæsthesia, ether and oxygen, may be given, but there are always two disadvantages: the recurrent laryngeal nerve cannot be spared with certainty, and the sickness after the operation, considering the slow coagulation of the blood, makes the healing slow, and has a bad general influence. The local anæsthesia is done by injections of $\frac{1}{2}$ and 1 per cent. novocain solution with 2 drops of 1 per cent. adrenalin solution for 10 grm. of novocain. This is injected under the skin at the place of the incision, in the muscles where they are to be cut, and in the periglandular tissue, especially at the upper pole. It is important to calm the patient before the operation, not so much with drugs such as veronal, medinal, codein, and valerian, but more by mental influence. I can assure you that during the above-mentioned preparatory rest cure

in the house, which lasts from two to several weeks, we nearly always influence the patient so that he is anxious to have the operation and fears it no more. After most operations, even if not the slightest irregularity, not to speak of complication, takes place, when no antiseptics and no general anæsthetic have been employed, the patient shows a very severe reaction; the more so, the more severe the case is. Rise of temperature and pulse-rate, irregularity of pulse, albuminuria, glycosuria, restlessness, sweating, and oppression are quite usual, and sometimes very alarming. We find this reaction sometimes even more severe after ligation than after partial removal. If antiseptics have been largely used, or if the wound has had to be packed with gauze, or general anæsthesia has been given, this reaction is much more severe. On four occasions, in cases where we have had to give general anæsthesia because of the lack of self-control of the patient, we have seen this reaction go on for a period up to twenty-four hours, and ending in coma and death; and here the necropsy revealed fatty degeneration of the heart muscle, kidneys, and liver, with circumscribed necrosis, such as is found experimentally in the liver after chloroform death. Besides cases of death following the operation under general anæsthesia we lost 5 patients from pneumonia, 3 from nephritis (extensive fatty degeneration), 2 from embolism, and 4 who died, with the above-mentioned symptoms, very suddenly, and showed marked status lymphaticus, together with fatty degeneration, at the necropsy. If you consider the cause of death in all these cases and compare with it what I said of the special attention that must be paid to the condition of the heart, liver, kidneys, adrenals, lymphatic organs, and blood, before operating, you may conclude that the majority of deaths could have been avoided. If we had omitted general anæsthetics in the four cases, if we had refused to operate on the three patients who had distinct signs of kidney degeneration before, and on the four patients who showed status lymphaticus in very marked degree, all these would have been spared, and our statistics showing 2.6 per cent. mortality from 865 operations would be only a little over 1 per cent.

We come to the conclusion that early diagnosis of Graves's disease is the important task of a medical man. If this is established an early operation should be performed by an experienced surgeon. After the operation treatment with rest, proper food, good air, especially mountain air, avoiding any nervous or toxic influence, will bring about radical cure in a fairly short time. Thus we shall not only avoid recurrence of the disease, but the patient will be spared the toxic influence on his heart, kidneys, and liver, of which he will die sooner or later. The

thyroid gland will resume its normal function, whilst, if the disease is progressive, it may reach such a point that the gland is no longer able to do so. In severe cases and in those of long duration a careful examination, according to our modern knowledge of the disease, must be made. Cases with distinct symptoms of functional degeneration cannot be operated upon without risk. Only surgeons who have great experience in the surgery of the neck, who are able to make complete hemostasis, and who can guarantee complete asepsis, should operate in Graves's disease. A difference should be made between cases of goitre with symptoms only of Graves's disease, and the progressive full disease. The results of operative treatment in the first should not be published as results of operation in Graves's disease, without adding that they were rather cases of hyperthyroidism grafted on ordinary goitre.

MR. WILFRED TROTTER: My contribution to this discussion is made with a good deal of diffidence and hesitation, because my experience of the operative treatment of Graves's disease is quite a small one, and I regard many of the most interesting problems of the subject as being so far from solution as not profitably to be entered upon here. Limited as one's experience is, and it is based on less than fifty cases, it has enabled one to come to certain rough practical conclusions which I will attempt briefly to put before you.

In comparing the medical and surgical treatments of Graves's disease it must be kept clearly in mind that the former does not attempt to influence directly the course of the disease, but is limited to putting the patient under favourable conditions while the disease runs its natural course, to end in arrest, spontaneous cure, or death. Operative treatment, on the other hand, is intended to be specific and to deal directly with the disease itself. It is clear, therefore, that we have to take into account not merely the comparative mortalities of the two methods, but also the length of the natural course of the disease and the condition of the patient during its progress. That the condition of a patient with severe Graves's disease is a very miserable one is common knowledge, and is strikingly shown by the willingness of the patients to submit to operation, although they are rendered morbidly nervous by the disease and have usually been told before they come to the surgeon that the operation is an excessively dangerous one.

While I do not attempt to minimize the fact that the mortality of the operation is a considerable one, and possibly greater than that of the untreated disease, I am convinced that it would be justifiable to run a good deal of risk if it were the means of avoiding the years

of miserable illness which are the lot of so many of the patients. It seems to me, therefore, that now we know the operation can be done without, at any rate, a very great mortality, the principal interest centres round the results rather than around the actual death-rate. I confess that to me discussions as to the relative death-rates of the untreated disease and of the operation—now we know that they are not widely different—seem to be comparatively useless, whereas the question of what relief can be obtained by operation is of the utmost importance. Unfortunately it is a most difficult question to solve in a way satisfactory to any fairly sceptical inquirer.

There is no disease more difficult to deal with statistically than exophthalmic goitre. Not only does the fully developed disease include certain well-defined types, but this central group is surrounded by very numerous forms which constitute an unbroken series, from unmistakable Graves's disease on the one hand to wholly non-toxic goitres on the other. It is the actual difficulty in drawing sharp lines of distinction which makes one look upon all statistics of the disease, surgical or medical, with a certain caution. The same ambiguity renders the statement of results equally difficult to interpret. Anyone who has some experience of the operative treatment knows that all grades of relief are met with, from total and permanent disappearance of all symptoms to the mere temporary subsidence which follows all operations. To divide the results into classes according to cure, much improvement, no improvement, seems to me to put much too great a strain upon the judgment of the observer, and can only be of any considerable value when the material dealt with is of enormous size.

Again, the selection of a single objective sign such as pulse-rate, exophthalmos, or body-weight, as a measure of improvement is open to equally serious objections. Exophthalmos or tachycardia may, as is well known, become stereotyped and persist as an isolated phenomenon while the patient is perfectly well in every other respect. The body-weight is at first sight a more valuable standard. Experience has shown me—though I do not believe the fact is generally recognized—that the body-weight may show abnormal variation in *both* directions in Graves's disease—a pathological diminution being succeeded by a pathological increase, or vice versa.

I may mention two cases which illustrate how fallacious a mere record of weight may be. In each of them the first sign of disease the patient noticed was that she became very fat. As the disease developed severe emaciation came on, and at the time of the operation both patients were extremely wasted, the weight of one, for example, having

fallen from the abnormal figure of 11 st. to below 6 st. In each case after the operation the patient rapidly put on flesh, and there was great improvement in all the symptoms. Then a stage was reached when the patient was uncomfortably fat, and though much better than before, yet had a distinct residuum of symptoms. A second operation was now done. Following it all the symptoms completely disappeared, and the patient actually lost weight, the one in whose case I have given the figures losing over a stone and settling down to 10 st., her normal weight.

In view of these and similar facts it would, in my opinion, be useless for me to attempt to set the results of my small experience before you in tabular form, and I shall therefore merely try to give as frankly as I can such practical general conclusions as I have come to.

In the first place I propose to deal shortly with the question of mortality. The operation is one which shows a marked contrast with all other operations on the thyroid. Of these latter, as is well known, there is practically no death-rate. In a considerable experience of thyroid operations, excluding exophthalmic goitre but including a fair proportion of malignant and of intrathoracic goitres, I have never lost a case from the operation, and that, of course, is the common experience. Graves's disease, on the other hand, shows a mortality which was in the early days heavy and is even now considerable. The mortality, however, presents this encouraging peculiarity, that it can be, and invariably is, reduced as the surgeon acquires experience in the special requirements of the operation.

Taking the experience of representative surgeons on the Continent, you will find that out of the first fifty cases of any given surgeon he will usually lose five as a direct result of the operation. This 10 per cent. mortality is usually considerably reduced in a surgeon's later work, and is no doubt to some extent to be regarded as a measure of the difficulty in acquiring the special kind of knowledge which goes to successful operating on these cases. I should be inclined to venture the opinion that a reduction to 5 per cent. should be generally possible, and I think that if that could be established as a standard figure, the operation could be regarded as having made out at any rate a strong *prima facie* case for being tried on a large scale.

In my own cases I have had a mortality of 10 per cent. This is undoubtedly, as I have already said, a high figure, and I may add by way of comment that it is based on a strict definition of the disease and an unwillingness to admit the larval forms except on very good evidence. Moreover, I have never felt justified in refusing to operate on a patient on account of the severity of the symptoms, for it is just the worst cases

which are most urgently in need of relief and for which if the operation is survived the most brilliant results can be attained.

Turning now to the results, one may begin with the general statement that all patients who get over the operation show some more or less permanent improvement, while in some all symptoms disappear as if by magic within a few days.

The two most definite statements one can make are, first, that patients with a small firm thyroid and marked symptoms scarcely ever show more than a temporary improvement. In them the operation is never seriously dangerous and never really satisfactory. The class is not a large one; I have dealt with not more than three or four definite cases.

Secondly, early mild cases—that is, cases without an abrupt onset, and showing a well-marked interval between the appearance of the physical signs and the development of the symptoms—invariably do well and are cured by a single operation. This class is well defined, easy to identify, and allows of a positive prognosis being made. They constitute about a quarter of my material. The operation seems entirely free of danger, and no such case has ever given me any anxiety.

The bulk of the cases—more than half my material—presented the disease in a severe form, the symptoms being marked as well as the physical signs and the goitre well developed. In such cases the improvement seems to vary with the amount of thyroid removed, and in about half of them is permanent and more or less complete. A second operation may be necessary because of a residuum of symptoms being left or because a recurrence takes place. I am inclined to say of this class that at least half can be permanently cured, though some need a second operation to secure this result. Of the rest, the disease can be greatly relieved or brought to a standstill in most.

Anything more detailed than this rough analysis would not, in my estimation, at the present time be of much value, but I should like to add that I am deliberately giving cautious and conservative estimates of the results.

To turn for a moment to the more technical aspects of the subject, I should like to add a few words as to anæsthesia and technique of operating. I have used chloroform, open ether, ether by intravenous infusion, and local analgesia.

There seems to be a strong current of feeling at the present day against the use of chloroform in these cases, and I must admit that I have been influenced by it. There can be no doubt that the drug is more toxic than ether, and I feel that we are not justified in adding any risk, however small, to those necessarily contingent upon the operation.

Still, I should like to say that in all my earlier cases chloroform was used and gave satisfactory results in some of the severest. The pulse-rate practically always diminished during the anæsthesia. Of course, such an anæsthetic should never be given except by the most accomplished expert, and I was fortunate in having for the most part the assistance of my friend Dr. Herbert Scharlieb. Ether by infusion I do not regard as presenting any considerable advantage except possibly in the elderly, where pneumonia is to be feared.

At present I rely entirely upon ether by the open method in combination with atropine, morphia, and scopolamine, and in certain cases upon local analgesia. In connexion with the use of ether, I should like to lay stress upon the importance of the preliminary atropine and upon the anæsthetist satisfying himself that this drug is acting before he begins the anæsthetic.

With regard to the actual operation, the choice of the time for its being done is in my opinion very important. I do not, however, acquiesce in the view that has been expressed that the patient should be submitted to several months' medical treatment as a preliminary. After all, this merely means watching the course of the disease for such a period, and I think that after some experience one can estimate the type of the disease and the course it is likely to follow without an expenditure of time so discouraging to the patient. As to the existence of an acute exacerbation, I should not hesitate to operate at such a time if I thought the patient's life was being endangered by the condition, though as a general rule it would be better to wait. Bronchitis, tonsillitis, and acutely inflamed cervical glands, which are common complications, I regard as absolutely contra-indicating operation for the time.

I have come to regard the mental state of the patient as perhaps the most important feature of the case in prognosis both as to the danger of operation and as to the final result. All the patients are nervous—that is, of course, part of the disease; but not all are frightened, and the really frightened patient is the most dangerous of all. To explain this, I do not think it necessary to invoke the changes in the cerebral cells of frightened animals described by Crile. A much simpler explanation seems to me available. Fear acts by precipitating an access of tachycardia during which the pulse-rate is perhaps uncountable for hours. In such circumstances the anæsthetic does not produce the usual steadying of the pulse, and the shock of the operation or the least amount of cyanosis from laryngeal spasm may be fatal. It is in these cases that the modern method of ether administration is so valuable. In hospital nowadays, in my cases, the patient is always anæsthetized in bed in the ward.

In the actual operation itself speed is no doubt valuable, but it is much less important than gentleness of manipulation, which is absolutely indispensable. A large incision is essential to give easy access to the gland, and any kind of pulling is to be strictly avoided. In getting out the upper pole traction is very easily transmitted to the superior laryngeal nerve, with the immediate result of causing laryngeal spasm and cyanosis—a most dangerous complication. Drainage is sometimes necessary when the anæsthetic is ether, to allow of the escape of blood. Otherwise I never use it, and I have not seen the slightest evidence that the thyroid secretion can cause symptoms by being absorbed from the wound.

The operation done in my cases has always been a partial thyroidectomy, usually the removal of one lobe and the isthmus.

The chief causes of death are shock during or immediately after the medical operation, an exacerbation of the disease within the next twenty-four hours, or pneumonia in the first week. I have lost two patients from shock, one from an acute exacerbation and one from pneumonia, and I am convinced by the study of that experience that the danger of the occurrence of such complications can be greatly reduced. This is to be effected by adequate mental and physical preparation of the patient, the choice of the best time for operating, the right anæsthetic for the given case, and the most careful avoidance of any traction upon or crushing of the gland. Such conclusions have been entirely borne out by my later experience.

Dr. DUDLEY BUXTON remarked that so much had been said by other speakers that it would not be necessary for him to address the meeting at any great length; and he proposed to confine his observations to the question whether local analgesia or general anæsthesia should be employed. The objections advanced against the employment of general anæsthesia in the case of Dr. Dunhill were inadequate, for he appeared to have had an extremely small experience of its uses, and therefore his results went for little in this regard. Professor Kocher also appeared to have lent the weight of his great name to the employment of local analgesia, and, having been contented with that, he had sought but little aid from general anæsthesia, while in the cases in which it was employed he appeared to have been singularly unfortunate. In estimating the value of any method, it was important to investigate how the method was carried out, whether properly or improperly, and whether the quantities of anæsthetic given were adequate without being excessive. In examining the question from

that standpoint one arrived at the explanation of the discrepancies in the views of those who, on the one hand, advocated local analgesia, and on the other general anaesthesia. In the case of local analgesia one found certain surgeons expressed their admiration for it because they were accustomed to work with it, and it supplied them with what they needed. But that was no just argument in favour of local analgesia nor, indeed, was any argument needed in its favour. It went without saying that it was a very valuable method when properly carried out. Whether in all cases it actually brought about the advantages claimed for it he had yet to be convinced. Certainly some patients suffered pain during the performance of the operation. That might be due to failure in technique. Some of them also suffered much pain afterwards, as well as insomnia, and this was a great disadvantage. Further there was the grave danger of psychic shock: many patients, especially those grouped under the heading of status lymphaticus, were liable to sudden death through this or even from fright, and many persons had so died. It was certain that some surgeons did not realize how profoundly the nerves of their patients were affected under local analgesia.

One of the benefits of general anaesthesia, if properly conducted, was the after-sleep which these patients enjoyed, and this, he submitted, made for recuperation. Then it had been said against general anaesthesia that the after-effects were severe, the vomiting bad, and that there was a likelihood of tissue poisoning—misnamed post-chloroform poisoning—and various other undesirable sequelæ. He invited his hearers to consider these. He had had a wide experience of general anaesthesia in relation with the cases under discussion, but he had not met with these after-effects, and for that reason, perhaps, he required more proof of their constant occurrence than was offered by those who, in a few cases, had met with the misfortune of losing patients from this form of tissue poisoning. He submitted that bare statement was no proof as against general anaesthesia.

With regard to his own experience—experience was of most use in such a discussion—he stated that for many years he employed chloroform in cases of goitre. He agreed with Mr. Trotter that chloroform was a more powerful narcotic drug, in the toxic sense, than was ether, and being a protoplasm poison, it stood in the position of being capable of doing more harm. But he believed that chloroform would do harm mainly when employed in quantities which acted as a poison, not when employed in quantities which merely acted as an anaesthetic. He contended that when chloroform was employed in such a manner as to merely produce an anaesthetic effect, without

overloading the tissue with what was certainly a poison, there was little fear of post-operative toxæmia due to the anæsthetic—chloroform. He considered that the whole question depended upon whether the anæsthetic was properly given, whether the anæsthetist had had an opportunity of examining the patient beforehand, and deciding upon the line he would pursue in dealing with the case, and selecting the proper method. He could then avoid over-dosing the patient, by bearing in mind that the patient was already toxæmic, and that if this disability were added to by the unwise use of the anæsthetic he would jeopardize his life. The danger which was commonly overlooked was asphyxia. This danger could be obviated by the method he (Dr. Buxton) had adopted, of using oxygen *pari passu* with chloroform, the latter being given in every case by the dosimetric method. It was important that the patient should be in the third degree of narcosis—as it was necessary that these patients should not be operated upon until they had been fully anæsthetized—then there should be a lightening of the narcosis to the second degree, the laryngeal reflex being present so as to prevent asphyxial complications.

It had been pointed out, and was now common knowledge, that all these thyrotoxæmic patients suffered from a condition of extreme nervousness and nervous exhaustion, and in many cases to this was added fright. That complication, he considered, was best met by putting the patient to sleep before the anæsthetic was given by a preliminary hypodermic injection of scopolamine, morphine and atropine; then she passed from the dream-sleep into the sleep of anæsthesia. When that method was adopted, the anæsthesia in these cases presented no more danger than it did in the case of any person suffering from auto-toxæmia. In studying the details of a large number of patients who had been submitted to his judgment to decide if they could safely be given a general anæsthetic, he found he had never been compelled to refuse it. Twice he had advised postponement, once to allow a fortnight's rest and medical treatment, and once because the patient was suffering from post-influenzal bronchial catarrh. He had never met with any fatality—the result of the anæsthetic, or any case the after-study of which had made him regret adopting a general anæsthetic rather than a local analgesic. As to the choice of anæsthetic, for many years he employed chloroform, more recently he had used the open ether method, but always in association with atropine, generally with atropine, scopolamine and morphine. He thought that the intravenous infusion of ether method held out hopes of proving extremely useful in such cases. But the employment of ether was open to the

—possibly theoretical—objection that the condition of the patient under it seemed so extremely good that sometimes the surgeon was inclined to operate for a greater length of time and do a more elaborate operation than he would have done if the patient had appeared to be in a less happy condition. Then so soon as the unnatural stimulus of the ether passed off, the patient showed marked collapse and might, as a result, gradually sink and die.

The speaker submitted that most of the arguments against the use of general anaesthetics were true only as against faulty methods and inexpert anaesthetization. If local analgesia was applied by a faulty technique—and it not infrequently was so applied—and failed, its value was not impugned, but a faulty technique was justly assigned as the reason of the failure, while in the case of general anaesthesia failure, bad after-effects, even fatalities, were at once accepted as inherent to the anaesthetic and no attempt was made to investigate whether the technique was at fault or the inexperienced person responsible for the narcosis had transgressed the canons of procedure accepted by those possessed of wide experience in dealing with cases of anaesthesia in the surgery of exophthalmic goitre.

Mr. HERBERT J. PATERSON, as a preliminary to his remarks on the subject, showed three patients on whom he had operated. He had asked several to come up. One case would be classed as hyperthyroidism, but she had all the symptoms of Graves's disease except exophthalmos. None of the patients were absolutely cured, although all were greatly benefited. The first patient shown was aged 33, and was operated upon two and a half years ago. She had a swelling of both sides of the gland, and her chief symptom, in addition to a rapid pulse, was continuous vomiting for four years. She had no exophthalmos. She was now much better, but not absolutely well. The next was a more recent case, the patient being operated upon last summer. Before operation her pulse was 190, and that rate was reduced by medical treatment and rest to 140. Before operation she had marked exophthalmos, which still existed but was not so severe now. She no longer suffered from attacks of palpitation and was much better. Another of the patients was 41 years of age, and had undoubted Graves's disease, with fairly marked exophthalmos, and much swelling on both sides. When looking in certain directions she still had some exophthalmos and a lagging in the movement of the eyes.

(The Discussion was adjourned until March 5.)

Surgical Section.

JOINT MEETING WITH THE MEDICAL SECTION AND
SECTION OF ANÆSTHETICS.

March 5, 1912.

Dr. W. J. McCARDIE, President of the Section of Anæsthetics,
in the Chair.

Discussion on Partial Thyroidectomy under Local Anæsthesia, with Special Reference to Exophthalmic Goitre.¹

MR. A. E. BARKER: After due study and some experience, I do not think a good case has as yet been made out for operative interference in well-marked cases of exophthalmic goitre, whatever may be said of operation for some thyroid tumours associated with milder forms of thyroidism. I must confess that the able and interesting papers to which we have been privileged to listen in this room have not altered my attitude, though they have made it more difficult for me to differ from surgeons who for one reason or another have operated for this disease much more frequently than I have done. Indeed, Dr. Hale White's admirable and ingenious way of putting the case has decidedly strengthened the feeling I have been driven to. The intrinsic difficulties of the operation are obviously not the deterrent. Those of us who are constantly dealing with all varieties of thyroid tumours are familiar with them and able to surmount them. It is, in a word, the effect of the thyroidism as expressed in the nervous system that we have to fear, and the great liability to fatal shock from operations which without the thyroid intoxication would produce no shock. These dangers from collapse, I fear, are not likely in the future to be overcome in cases where thyroidism is well advanced, that is, in the class of cases which

¹ Third meeting (adjourned from February 27).

do not yield to medical treatment, and they will keep up the mortality after operation probably to the same level as that among those not operated on. Dr. Hale White's interesting analysis of a large number of cases treated medically shows, if I understand him rightly, a mortality for exophthalmic goitre of 15 per cent. But the death-rate among a similar number of ordinary people of the same ages would have been, as stated by an actuary, $7\frac{1}{2}$ per cent. This seems to show, as far as it goes, that the deaths from Graves's disease treated medically were in his list only from 7 to 8 per cent. above the death-rate for the same number of people of the same age not suffering from exophthalmic goitre, and his series would almost certainly in the nature of things contain more of the severe cases than any series operated on. Mr. Trotter's careful analysis of his fifty cases gives, I think, a mortality of 10 per cent., which is, to say the least of it, no improvement on Dr. Hale White's results where no operation was done. In all series of cases treated by operation milder cases which would give the best prospects of being cured by rest and drugs without surgical operations are sure to be included; and their inclusion will naturally diminish the gross mortality from operation. Moreover, a good many cases operated on are apparently not cured and require further treatment. It is also fair to conclude that part of the good effects following operation may be due to the enforced rest before, during, and after, for a considerable time. These are some of the considerations which, among many others, have led me to the conclusion that a clear case has yet to be made out for operation on cases with marked thyroidism.

As to the form of anæsthetic to be employed, if an operation is done one cannot fail to be impressed by the very large experience of the Kocher school, where local analgesia is almost exclusively used. In most of my own thyroid operations I, too, have resorted for many years past to local analgesia, and have been well satisfied with it, although in certain cases general anæsthetics of various kinds, chloroform, ether, with scopolamine and morphia, have been had recourse to. But then, as I have said, my experience includes relatively few cases of Graves's disease in its extreme degree. Nevertheless, it embraces many severe operations in which I thought general anæsthesia would have been dangerous, and no case has been lost where local analgesia has been employed. Candidly, however, the cases are different, and I can quite understand the feelings of those who hesitate to add to the excitement and agitation of patients with advanced symptoms of exophthalmic goitre by an operation during full consciousness. But that complete

and adequate analgesia can be obtained for this class of operations by local and regional methods combined, our experiences with deep-seated thyroid tumours jammed behind the sternum and clavicle amply prove. Each surgeon will have to decide for himself whether this is enough without total anæsthesia in highly excitable patients. If local analgesia is employed in these cases it must, I think, be combined with morphia, or some other efficient general sedative and must be carried out by one quite familiar with the details of the method and able to complete the infiltration quickly and efficiently in a way to gain the confidence of the patient. I am afraid this will usually have to be the surgeon himself, who knows the ground he will have to cover and the amount of force he will have to use in his deep dissection. This may appear at first sight a rather ungracious remark to make to an audience so largely composed of anæsthetists, but it is certainly not intended to be so. No one could feel more strongly than I do the great debt that all surgeons owe to the special anæsthetists who have done so much to make general anæsthesia safe for the patient and helpful to the operator.

Mr. CHARTERS SYMONDS said that before discussing the subject he would like to congratulate the Sections which had combined in what he thought could well be called a very important epoch in the operative surgery or the general treatment of exophthalmic goitre; and that feeling could be extended to Dr. Dunhill for raising such an important question. To criticize Dr. Dunhill's paper first, he thought it conveyed an impression of rather too much safety with regard to the operation itself. And, as Mr. Barker remarked, the cases in Dr. Dunhill's fourth class would probably be found to contain a good number which others would call cases of nervous patients with an ordinary goitre. Though in the second class he certainly gave the proportion of cases, it was a little difficult to form an accurate judgment on the relative mortality of the various classes. An important point to lay stress upon was the necessity of selecting cases, and of distinguishing between patients who were nervous and had a goitre and those who had true hyperthyroidism. In this connexion he might mention the case of a lady, aged 40, who for some time was thought to have exophthalmic goitre, and who showed practically all the symptoms except exophthalmos. Operation was delayed—as he thought, wisely—and he watched the case for a considerable time. At the end of a few months the right lobe became rather larger, the left diminished in size, and a localized tumour

appeared. This was successfully removed, and the patient got well. That was the kind of case which he had in mind, and if progress was to be made in the operative line of treatment it would be necessary to distinguish clearly between those cases which were likely to recover and those where the condition became progressively worse. In fact, finer distinctions were needed, based, perhaps, upon closer examination of the other organs of the body, and of the blood. A very important part of our work consisted in analysing the various classes of cases, and for that purpose he thought there should be a more frequent consultation between physician and surgeon, a practice which seemed to be somewhat neglected at the present day.

All who listened to the summary of treatment which was given by Dr. George Murray must have been struck by the great help any surgeon would derive from talking over a case with him. He hoped surgeons would look to those who were studying the medical treatment of such cases, for help in separating out the cases which could be safely operated upon. Again, he hoped the cases would be seen much earlier, for in that fact must rest the great success of the operation. It was found that amongst many men, at least those in general practice, there was still a great deal of apprehension as to the danger attending any thyroid operation. He believed that when people recognized that thyroidectomy in itself carried but little danger, that hyperthyroidism was the cause of Graves's disease, that wasting of a lobe would take place when the first lobe was removed, and that the disease could be safely operated upon in suitable cases, patients would be brought earlier, and there would be a possibility of placing the operation for that disease in the same realm of safety as ordinary thyroidectomy at the present day. He feared that, speaking generally, surgeons were a little too much inclined to operate on everyone, and in that respect the physician must take his share of the blame, for sometimes the surgeon was asked to open an abdomen when the physician seemed afraid to rest upon the obvious signs of disease. Clearly, no operation was without its risks, and although modern surgery was very successful, largely on account of asepsis and some training, all would recognize that risks could not be excluded. In the case of some operations, frequent performance was necessary to command safety, and in connexion with the particular operation under discussion it was necessary to possess that skill which was derived from general experience in operating. In this special case it was necessary to avoid haste, to proceed along very definite lines, to know when to leave a portion of the capsule of the thyroid, how to

avoid tracheal tugging, and how to make a new attack when the first had failed.

The profession should take to heart the counsel of Dr. Kocher and recognize that operations on goitre were not for those whose chief work lay in doing minor operations. He said that, because there was reason to fear that these operations might be done a little too freely, with a consequent increase in the proportion of failures. If it were possible to have a record of all the operations on cases of exophthalmic goitre which had been done during the last five years, he believed the mortality would be found to be such as to cause great hesitation in undertaking the operation. He had had some experience, but he still looked upon operations on exophthalmic goitre as serious undertakings, and considered much yet remained to be learned before success could be commanded. The successes of Dr. Dunhill and Dr. Kocher gave the idea that there might be some difference between the forms of goitre which those operators met with and those seen in this country. Again, it seemed to be more easy to persuade people in Germany and Switzerland to submit to the operation under local anæsthesia than in England. He had only been able to persuade two patients to submit to it, so that he was not so successful in that way as Mr. Barker. They did very well indeed. In all the goitres he had operated upon—parenchymatous varieties and the enucleation of cysts and adenomata—he had used chloroform, except on two occasions, and he had never had anxieties in goitre cases. He was speaking of other cases than malignant and exophthalmic goitres.

One of the great values of this discussion would be to enable a more correct estimate to be formed of the condition of patients, and a knowledge of the kind of case in which operation was likely to succeed. Still, those who listened to Dr. Kocher's paper must have been impressed by the remark towards its close, "that if one considered the cause of death in the cases and compared it with the special attention which must be paid to the condition of the heart, liver, kidneys, other organs, and the blood, before operating, it would be concluded that in many the deaths could have been avoided." He hoped in future more attention would be paid to those matters, so that the results of operation could be made more satisfactory.

MR. DONALD ARMOUR: My operative experience in cases of exophthalmic goitre comprises twenty-six cases, of which two are males and twenty-four females. Practically all my cases have been operated on

only after consultation with a medical colleague. I have had one operative death—a mortality of under 4 per cent. In the light of subsequent experience, this case should never have been operated on. She was in the last extremity of the disease, suffering from constant diarrhoea and vomiting and delusions, combined with extreme emaciation. The operation was performed as a last resort, medical treatment having failed to give her any benefit. This was the only case in which local anaesthesia was used. But the general restlessness of the patient made recourse to a general anaesthetic finally necessary. She died a few minutes after the operation had been completed and the dressings applied. The autopsy showed a condition of well-marked status lymphaticus.

In my first four cases I employed ligature of two or more arteries. I have now given up the ligaturing of arteries. The operation in some cases is more difficult than partial thyroidectomy, and the results not so certain. I always now perform partial thyroidectomy, removing one lobe and the isthmus, and a part of the second lobe if considered advisable. I always use the collar incision and dissect the flaps upwards and downwards very thoroughly. Section of the infrahyoid muscles near their upper attachments is carried out if necessary to allow an easy approach to the gland. These are carefully sutured afterwards. This section of muscle allows of early and easy ligation of the superior thyroid artery.

I consider the chief essential in the performance of the operation is to avoid all rough handling, squeezing or pressure on the gland of any kind. Crushing of the isthmus is especially to be avoided, as proved by one of my cases in which I used this method and in which the pulse was immediately accelerated to 180 beats per minute. Any cut surface of the gland or isthmus is painted with absolute alcohol and the capsule drawn over it with two or three sutures of fine catgut. Any attempt to shell out the lobe with the finger should be avoided. The capsule is gently wiped off the gland with gauze, as one separates adhesions in the abdomen. Any danger, if such danger exists, of injury to the inferior laryngeal nerve is thus avoided. Large quantities of saline are given by the rectum for at least two or more days after the operation, or subcutaneously if not retained *per rectum*. I only use drainage in very exceptional cases. My first twelve cases were collected by my friend Dr. Alfred Warren, and formed the basis of his M.D. Thesis at the University of Cambridge. I am greatly indebted to him for the care and industry with which he followed up these cases. I will quote his

ANALYSIS OF CASES.

Case	Classification	Onset	Duration	Course before operation	Operation	Result
1	Primary (vascular goitre); idiopathic	Sudden	7 months	Moderate severity; progressive; all four cardinal symptoms	Ligature three arteries	2 years 2 months after operation: Cured
2	Primary; idiopathic	Sudden; very acute	18 years	Well-developed case resisting all treatment for years	Ligature two arteries	2 years after operation: Distinct improvement and gain in weight; no active Graves's disease, but legacies; hypochondriac and neurasthenic
3	Primary; idiopathic	Insidious	5 months	Mild but progressive; all four cardinal symptoms	Ligature two arteries	2 years 2 months after operation: Cured
4	Primary (vascular goitre); idiopathic	Fairly definite; not acute	8 months	Moderate severity	Ligature three arteries	Distinct improvement for 10 months, then began to relapse; death from intercurrent disease 13 months after operation
5	Primary; idiopathic	Insidious	2½ years	Moderate severity; progressive in spite of treatment	Partial thyroidectomy	1 year 10½ months after operation: Very greatly benefited, almost a cure; circumstances prevented favourable after-treatment
6	Secondary	Insidious	2 years	Progressive enlargement of thyroid necessitating operation	Partial thyroidectomy	1½ years after operation: Greatly benefited
7	Secondary? infective	Sudden	9 years	Progressive; increasingly severe attacks of dyspnoea demanded operation	Partial thyroidectomy	1 year 9 months after operation: Cured
8	Primary infective	Definite	6 weeks	Palpitation a marked feature	Partial thyroidectomy	Remarkable benefit for 11½ months: Relapse and death 1 month later
9	Primary; idiopathic	Definite; not acute	18 months	Subacute symptoms with relapses	Partial thyroidectomy	Marked immediate benefit from the operation lasted 11½ months; then severe tonsillitis; a relapse from which she was improving 13 months after operation
10	Primary; idiopathic	Definite; not acute	2 years	Progressive, with exacerbations; nervous element pronounced	Partial thyroidectomy	Marked immediate benefit, which lasted 2½ months; then tendency to relapse
11	Secondary	Thyroid enlargement 17 years; symptoms 2 years	17 years	Mild case	Partial thyroidectomy	3½ months after operation: Improvement maintained to date
12	Primary	Definite; not acute	2½ years	Not a severe case, but patient tired of unsuccessful medical treatment	Partial thyroidectomy	Apparently benefited, but too recent to say more

findings as laid down in his Thesis (*see* Table). The cases operated on since, as far as I have been able to trace them, have either been very greatly improved or quite cured. Of these one is a man, a bookmaker by profession, who has been able to return to his arduous, and let us hope, profitable occupation. One of the women, a cook by occupation, writes she is perfectly well, and is able to do her work without trouble. Another is in charge of a large private hotel. Another, a nurse, who performs her duties without trouble; while another writes me, under date February 16, 1912, to let me know that, "I still keep quite well and have had no more return of my symptoms." She was operated upon on April 28, 1907. One of my worst cases, of whom my medical colleagues prophesied certain death if she was operated on, is now so well that she does her own housekeeping, and takes complete care of an invalid mother.

I will not refer to the question of anæsthesia, beyond saying that all my cases have been done under a general anæsthetic. The anæsthetic has been administered, in practically all my cases, by Mr. H. M. Page, who is present and will add to my remarks his own in reference to the subject of anæsthesia.

MR. WALTER EDMUNDS: Both physicians and surgeons will agree as to the value and practical importance of Dr. Dunhill's paper. He divides the cases into four classes, and in his fourth class he places cases of adenoma of the thyroid gland with some tremor, some staring of the eyes, and an easily excited heart. These cases should, I submit, be regarded as undoubted cases of Graves's disease, for they have both its symptoms and its pathology. Several years ago I operated on a case of enlarged thyroid with tremors, palpitation, and a slight degree of exophthalmos. An adenoma was found and removed; the patient quickly got well, and remained so for nine years. Then the thyroid again enlarged and the symptoms, but without exophthalmos, reappeared. Another adenoma was removed, and the symptoms at once disappeared. The adenomata removed in this case, certainly on the first occasion, showed the usual hypertrophic changes. Similarly a friend has recently given me a section from an adenoma of the thyroid which had been removed from a patient with undoubted symptoms of Graves's disease, including exophthalmos; the patient quickly got well, and the microscope showed the characteristic changes. Dr. MacCallum, who examined the tumours from the cases of Graves's disease operated on by Dr. Halsted, describes one in which there was well-marked exophthalmos

and in which there was found an adenoma which was removed with a neighbouring portion of the thyroid; the characteristic changes were found in the adenoma, but not elsewhere. But adenomata play a part also in well-marked cases of Graves's disease (Dr. Dunhill's Class I). In one case of Graves's disease which came under my care, there was an unsymmetrical swelling of the thyroid suggesting an adenoma or cyst, and partly on this account an operation was recommended. An adenoma was found and removed, but there was, in addition, a general enlargement of the gland, part of which was also removed; the adenoma was breaking down in the centre, but the outer part showed the usual changes. The exophthalmos and other symptoms disappeared, and the patient remained well for a year, but latterly has not been quite so well. In another case under my care, which has not been operated on, but improved under various treatments, the X-rays seemed to produce a reduction of the lateral lobes, and thus brought into prominence a hard central mass, which was unaffected by them. There is a very interesting case of the disease recorded by Mr. Newman, of Bishop's Stortford. The patient was extremely ill, and the only remedies which seemed of use were sour milk and X-rays. The patient recovered, the right lobe of the thyroid became of normal size, while the left lobe was the site of an adenoma the size of a tangerine orange. Apart from definite adenomata which can be shelled out, the goitre of Graves's disease often consists of different lobules in various stages and degrees of structural change. Presumably only those parts showing the hyper-secretory changes are responsible for the special symptoms. In the only other case in which I have operated, the isthmus and right lobe were removed. The patient, who, in addition to the usual symptoms, had spasmodic attacks of dyspnoea, was greatly benefited in all her symptoms by the operation, though not absolutely cured. This patient had been gradually getting worse under treatment. The operation was undertaken on account of the dyspnoeic attacks, which, however, did not appear to have been due to pressure.

I have recently published a series of cases which have been under treatment by myself or others with milk from thyroidless goats and with other remedies, but without operation. Thirteen cases are available for analysis; of them, ten are much benefited or quite well, one may be said to be about the same, although at one time she was much better, and two are dead. Of the ten cases many, no doubt, could have been operated on and if they had been they would probably have been nearly or quite well sooner. The case described as "about the same" might

have been operated on, and if all had gone well, she would probably have been better than she is at present, or well. But the most important question is about the two patients who have died. It is very doubtful if there ever was a stage in either case in which the patient could have been operated on. In the first case, No. 3 of the published series, a unilateral exophthalmos came on nine years before the goitre, and eight years later there was an attack of unconsciousness, followed by convulsive movements of one arm; further, the goitre, when it appeared, grew with great rapidity; it seemed to come almost in one night, and became very large. Similarly, the other case (No. 18 in the series) was a very severe one, a bad prognosis was given early in the disease, and even then the patient was too ill for operation; the family history also was bad, for a sister had previously died of the disease. Neither of these cases can be regarded as simply suffering from over-secretion of the thyroid gland, the indication being to remove a portion, and hope that the part left will atrophy.

The third class contains cases in which the thyroid is throughout greatly affected with the hyper-secretory changes. If a complete removal were attempted, the parathyroids would probably be removed too, and a fatal tetany very possibly started. If, to avoid this, a subperitoneal implantation of a parathyroid be proposed, it must be remembered that Halsted found in his experiments that for the operation to be successful it was necessary that the parathyroid should come from the same animal. The reason why, happily, none of Dr. Dunhill's patients have had tetany is probably because one or more parathyroids were left intact. A dog will live in good health with only one parathyroid, whereas if all are removed he will, unless treated, almost certainly die in a few days. By the continued administration of calcium salts his life may be preserved for months, but he will still die as a result of the operation.

As regards exophthalmos, Dr. Dunhill makes an important observation when he notes that the eye corresponding to the completely removed lobe recedes much more than the other. I have noticed the same thing. Unilateral exophthalmos is not very rare; there are said to be 109 cases on record. Administration of thyroid can cause exophthalmos, but Gley has exhibited two thyroidectomized rabbits with slight symptoms of myxœdema and also well-marked exophthalmos. Gley attributes the symptoms of Graves's disease to dysthyroidism. In the case of these rabbits there would be no thyroid secretion, but there would be unbalanced parathyroid and other secretions.

As to operation, my three cases did very well, and were greatly

benefited or cured; they all had a general anæsthetic. The choice between a general or local anæsthetic should be made on general grounds; if the former is decided on a good anæsthetist is especially desirable. The indications for the operation are: (1) asymmetry of and unequal consistency of the goitre suggesting an adenoma; (2) the case not yielding to medical treatment; and (3) threatening of ulceration of corneæ.

Dr. J. BLUMFELD: Advanced cases of Graves's disease such as Dr. Dunhill includes in his Class II are, I think, rightly regarded as amongst the most dangerous for general anæsthesia; and, soothing though it must be to the anæsthetist to listen to remarks such as those of Sir Victor Horsley and Mr. Leedham-Green, who declared the anæsthetic to be never culpable in operation fatalities, yet that appears to be too favourable in opinion. The subjects of this disease are liable to fatal heart failure apart from operation, but such failure has occurred during the early stages of anæsthesia, and it is then impossible entirely to exonerate the anæsthetic. This tendency is similar to and is as unexplained as that which is found in the much debated cases known as status lymphaticus, and it is at least interesting to note in this connexion the frequent occurrence in Graves's disease of an enlarged thymus, which is also, of course, a prominent feature of the other condition. The risk of anæsthesia, then, in these cases must, I think, certainly be regarded as above the average, but I do not think it is such that anæsthesia need ever be refused in a case which the surgeon finds fit for operation; at any rate, that is my own experience. Nor must it be overlooked that the temperament or nervous condition of these patients may make unconsciousness particularly desirable. How much value is to be allowed to the factor of what has been called psychical shock is very variously estimated, but in these cases it probably has considerable importance, and at any rate it is a factor that nothing but unconsciousness can remove. Some surgeons, Dr. Crile in particular, lay much stress upon the necessity of combating this factor, and I need not remind those here who heard him, at the British Medical Association's meeting two summers ago,¹ of the elaborate rehearsals in anæsthesia which he recommends before operation upon cases of Graves's disease.

I believe it is possible to achieve safety in these cases by shorter and simpler measures. The best method, in my opinion, is by the use

¹ *Brit. Med. Journ.*, 1910, ii, p. 758.

of open ether, preceded by sedative hypodermic injections. I use a combination of omnipon $\frac{1}{4}$ gr., scopolamine $\frac{1}{100}$ gr., and atropine $\frac{1}{120}$ gr. The injection is given one hour before operation. The patients usually complain of feeling dizzy and of dryness of the mouth, but they are often sleepy and always in a condition from which fear and apprehension are absent. They inhale the anæsthetic without discomfort. There should be no attempt, to my mind, at a very deep degree of anæsthesia for these cases. A degree is reached sufficient for the skin incision to be made without producing reflex movement, and after this the anæsthesia is so regulated that there is coughing or holding of the breath if the trachea or thyroid cartilage be dragged upon—these symptoms are unaccompanied by danger during the inhalation of ether. Used in this way, I do not think ether is open to the objection of causing congestion and increased bleeding; the atropine prevents any marked secretion of mucus, and there is, I think, an element of safety about the process which is not to be reckoned on in the case of chloroform, even if given dosimetrically and with oxygen.

Dr. SCHARLIEB, C.M.G., said that as he considered that chloroform and ether were so safe, and that as patients with exophthalmic goitre were so very nervous and very liable to psychic shock in his mind, those facts constituted an argument against the employment, in these cases, of local analgesia. If a general anæsthetic were given, the first thing to insist upon was that the patient should have, half an hour before the operation, $\frac{1}{100}$ to $\frac{1}{30}$ gr. of atropine hypodermically; the patient should be allowed to assume any posture he or she wished, and should be allowed time to get breath after being placed on the table. A commencement should be made with a mixture of chloroform and ether, or chloroform and absolute alcohol, avoiding the use of any apparatus. A change could then be made to open ether or chloroform, administered by any dosimetric method such as the Junker or the Vernon Harcourt. The anæsthesia should be of full degree for the first incision, and afterwards should be kept as light as possible. The anæsthetist appreciated the gentleness of the operators, and the minimum of traction exerted, as well as the speed of operating. He advocated deepening the anæsthesia again a little for the final suturing. He considered that open ether was preferable to chloroform. In these operations it was necessary to give atropine with or without omnipon or scopolamine, or scopomorphine, and to have the anæsthesia as light as possible.

Dr. G. A. H. BARTON: For some four or five years past I have taken a special interest in the subject under consideration. That interest was aroused by reading that the use of local anæsthesia was being adopted and advocated by Professor Kocher. It appeared to me that, so far as my experience went, this plan had no special advantages over general anæsthesia, and I resolved in future to record all my cases in order to compare the results in the two methods. At the same time I thought I might ascertain for myself what precise method of general anæsthesia secured the best results. I regret that the amount of material has so far not been very abundant, and I have notes of thirty-three consecutive cases only, not enough, I agree, to found any very strong opinion upon, but as far as they go they support my view that these cases can be managed quite safely and satisfactorily under general anæsthesia, and they have also led me to certain tentative conclusions as to the best method to be adopted.

Now I take it that there are two main dangers that may arise during anæsthesia in these cases—viz., circulatory failure in cases associated with Graves's disease, and asphyxial troubles in cases when there is pressure on the trachea or fixation of the cords. As regards the former danger, I may say that I have not met with it. Of my thirty-three cases, eight were cases of Graves's disease corresponding in the main to Dr. Dunhill's Class I, but many of the others would have come under his Class III or Class IV. In not one of these cases was there any circulatory failure, in fact, in most of them the pulse and colour improved under the anæsthetic. As regards the latter danger, there were eighteen cases which presented some history of obstruction of the airway; either there had been attacks of dyspnœa, or the trachea was shown by the laryngoscope to be constricted or displaced by the tumour. In one case, as the result of a former operation, there was some abductor paresis of the vocal cords. In two of the cases the tumour was removed in order to relieve these respiratory troubles, one of them being so bad that I approached it with the very gravest sense of responsibility. And yet what do I find in abstracting the notes? That out of the whole thirty-three cases some blueness was noted in five only, and in one some slight tendency to respiratory failure on pushing the anæsthetic. Of the five cases where there was blueness or duskiness (it never really amounted to cyanosis) it is distinctly stated in three to have been due to cough, retching, or holding of breath following too light an anæsthesia. Oxygen was only administered on five occasions. And here I may mention that one of the minor embarrassments of the anæsthetist is the

occurrence of cough, swallowing, holding of breath, laryngeal spasm, or retching. These symptoms arise partly from the necessarily faulty position of the head, extended over a sandbag, partly from the dragging on the trachea and nerves in the process of enucleation of a large or deeply embedded tumour, and partly from the difficulty, where inhalation anæsthesia alone is relied upon, of maintaining a sufficient degree of narcosis while at the same time keeping well out of the surgeon's area. Another minor embarrassment is the tendency for the tongue and jaw to fall back; in many of my cases the latter had to be held forward by a finger behind each angle during the greater part of the operation.

I will now briefly describe the methods I have employed:—

First as regards preliminary hypodermic injections. These were not given in the first fourteen cases, except that in one case $\frac{1}{100}$ gr. of atropine was given five minutes before the administration of the anæsthetic began. After this I began to use scopolamine and morphine injections, given generally half an hour to an hour before the operation, and sometimes combined with a little atropine. The dose of scopolamine was $\frac{1}{100}$ gr. and that of the morphine $\frac{1}{4}$ gr. or $\frac{1}{2}$ gr., according to physique of the patient. Cases 15 and 20, and 26 to 33 inclusive, were all treated in this way.

Secondly, as to the induction of anæsthesia. My usual practice is in ordinary surgical cases to use a mixture or sequence of C_2E_3 and ethyl chloride, the latter speeding up the induction and stimulating respiration and circulation. Ethyl chloride is not, however, advisable in thyroidectomy owing to the very frequent presence of a partially obstructed airway. I find that I only used it in seven cases. In the rest anæsthesia was brought about gradually by the C_2E_3 mixture followed by chloroform or open ether in some cases.

Thirdly, the operation having commenced, the sooner one can get rid of the mask and drop-bottle the better. The former may get in the way of the surgeon, and in any case each requires a hand from the anæsthetist which can generally be better employed. Junker's apparatus, which can be worked either with a foot-bellows or a slow stream of oxygen, was used in most of the early cases; the bottle was generally charged first with chloroform, but an effort was always made to add ether to this in increasing quantities. In some cases the resulting anæsthesia was too light, and recourse was had at intervals to the mask and the C_2E_3 mixture or chloroform, as circumstances seemed to dictate. In the later cases where scopomorphine was used a perfectly satisfactory anæsthesia was for the most part maintained by means of open ether given in an apparatus of my own which is self-feeding and obviates the necessity of a drop-bottle.

Now as regards results. In none of them, so far as the anæsthetic was concerned, was there the slightest real cause for anxiety. Twenty-cases were noted as excellent results, in most of which the pulse and colour distinctly improved under the anæsthetic. In eight cases there were minor difficulties from cough, laryngeal spasm, or retching, due, as I have said, to either too light an anæsthesia or to dragging on the deep parts during the enucleation. One case gave a little trouble in the following way: With a light anæsthesia there was trouble with cough, directly the anæsthetic was at all pushed respiration became somewhat shallow; this was one of the earlier cases. In two cases there was a very considerable amount of hæmorrhage, causing faintness, which had to be treated, one by a subcutaneous saline infusion. Had a local anæsthetic only been used in these two cases I fancy both the surgeon and the patient would have had a very anxious and uncomfortable time. Since using a preliminary injection of scopolomorphine I have only to note one case in which there was slight blueness owing to the presence of a scabbard-shaped trachea, and this was quite easily relieved by oxygen. In Case 31 the obstruction to the airway was so great that I administered oxygen throughout, and not the slightest cyanosis developed. Taking the cases as a whole, the best results were undoubtedly obtained when a preliminary injection of scopolomorphine was given and followed by open ether with or without the addition of oxygen. Very little anæsthetic is required, and the after-effects are frequently *nil*. I cannot say that I should advocate the use of ether where there is marked obstruction of the airway, as even open ether does occasionally cause some secretion of mucus and laryngeal spasm which might further embarrass the respiration.

Having regard to the extreme nervousness of these patients and the occasionally severe hæmorrhage, I think the balance of advantage is with a general anæsthesia, though I can well understand that there may be cases, as described by the previous speakers, so desperate as to contra-indicate its use.

MR. RUPERT FARRANT: Hyperthyroidism I take to be the main feature of Graves's disease. In this disease a *definite cycle* can be traced from thyroid excess to thyroid insufficiency. I wish to look for hyperthyroidism at the commencement of this circle, where it may be the most insignificant feature of any disease with which it is associated.

Group I—goitre cases. Here it is quite easy to picture a circle of

thyroid activity from Graves's disease, "formes frustes," thyroid enlargement with a few signs of excess, down to goitre cases with an apparently normal secretion or even insufficiency. This group of course includes the endemic goitres, and in any given case of commencing thyroid enlargement it is quite impossible to say to what height on this circle the hyperthyroidism may rise before it reaches insufficiency.

Group II—thyroid changes in other diseases. It is nearly twenty-five years ago since Dr. Hale White wrote a paper on Graves's disease occurring in association with other diseases. I will not mention any individual cases, but will simply mention three main classes:—

Dyspeptics.—I have examined some hundreds of these cases for signs of hyperthyroidism, and I have found that a definite thyroid circle can be traced from normal to excess, down to insufficiency. Here, again it is quite impossible to say to what height of hyperthyroidism an early case may rise.

Osteo-arthritis.—In exactly the same way, definite changes can be seen, early cases with excess, late cases with insufficiency, though for the most part these cases are seen on the down grade.

Mental Cases.—The first symptom of hyperthyroidism is nervousness. So I proceeded to examine some thousand lunatics for signs of thyroid changes. Without going into any detail as to the variety of lunacy, I may say that a definite thyroid circle can be seen running its course parallel with the mental symptoms. Nervousness, hypochondriacal depression and early insanity, with thyroid excess down to chronic insanity with thyroid insufficiency.

It is so easy to become obsessed when looking for anything one wishes to see, that these early clinical signs by themselves would be of no importance, but there is something to fall back upon, namely, the morbid histology. From the sections that I have made of thyroids in numbers of diseases, far from complete though they are, they show an hypertrophy more than corresponding to the clinical signs exhibited. It is these early cases of hyperthyroidism that form the spawning bed for Graves's disease, some of the cases running a small circle, others a larger one, and again others a big one and so reaching Graves's disease. These different cycles can be very easily watched. It is at the beginning of the thyroid circle that treatment should be commenced. Professor Kocher says that early diagnosis is essential in order that successful surgical treatment may be carried out. I should like to go one further and say that early diagnosis is essential for prevention of the disease. In all these cases showing thyroid excess a primary

toxic cause can be found. It may be an infected water supply, as in the goitre group, or it may be some definite septic focus, be it in the mouth, throat, nose, or intestine. Whichever it may be, on its removal there is an exacerbation of the symptoms followed by their gradual disappearance. Even these early cases do not take an anæsthetic well, not even gas for teeth extraction.

When the signs of hyperthyroidism have passed on unobserved to Graves's disease the primary cause can usually still be detected and removed, when the gland will involute, though a partial thyroidectomy will save the patient several years of invalidism. In the later cases the primary cause may have worked itself out and so not be apparent, but it will have always left indelible traces so that it can be easily detected. This is the way in which the disease normally cures itself, by the disappearance of the primary cause followed by involution of the gland. Certain cases recur after partial thyroidectomy, and this is put down to insufficient removal. True, but if the cause be first removed a smaller thyroidectomy will suffice. In the recurrences that I have seen the primary cause has not been removed and the remainder has gone on increasing.

The results of operation as claimed by different surgeons vary enormously. From the cases that I have seen and compared, it is those in the goitre group that give the best result from operation. This is in accordance with the results given by surgeons resident in endemic goitre districts. In London the cases mostly come under the second group. I have cases and slides to illustrate these various points, and they are slowly becoming more complete, and I hope to fully illustrate them at a later date.

In conclusion, I will sum up by saying that I think that if hyperthyroidism were recognized and treated one to three years earlier Graves's disease would cease to exist. I must thank the *British Medical Journal* for a grant to pay for the slides.

Mr. HERBERT J. PATERSON said that his experience, although small, was perhaps unique, as while he was anæsthetist at St. Bartholomew's Hospital he had given the anæsthetic in a number of these cases, and since then he had had surgical experience in them, so that he had been able to study the subject from the point of view both of the surgeon and of the anæsthetist. He took strong exception to the statement made by more than one speaker, that the administration of a general anæsthetic in these cases was unattended with risk; one

speaker qualified what he said by the remark "if the anæsthetic were properly given." He hoped the Chairman, as a distinguished anæsthetist, would agree that, no matter what the anæsthetic, or by whom given, the administration of an anæsthetic in Graves's disease was always attended with considerable risk. Chloroform, whether given by the open method or by one of the alleged dosimetric methods, was extremely hazardous, if indeed it was justifiable. If a general anæsthetic was given, he thought it should be open ether, preceded by morphine and atropine. He had himself seen six deaths on the table during operation on the thyroid gland, one in his own practice. He believed there were more deaths on the table during operations on the thyroid under general anæsthesia than in any other serious operation in surgery. He thought that the correctness of this impression would be verified by a perusal of the records of the London hospitals. It would be disastrous if one of the results of the discussion were to be that people were induced to regard general anæsthesia lightly. Mr. Symonds referred to the difficulty of persuading patients in this country to have local anæsthesia; he (the speaker) thought he should have said Londoners, not Britishers, because when he was at Cambridge he was much impressed with the readiness with which countrymen would come to the operating theatre and have big operations done without anæsthesia. He remembered one farmer putting his arm on the table for amputation, and saying, at the end of it, "Thank you." He did not agree with Dr. Scharlieb that the anæsthesia should be deepened just before the close of the operation; he preferred it to remain light, so that the oozing points could be seized and tied before the skin was sutured.

He had hoped that the discussion would produce a clear definition of Graves's disease; there was at present so much confusion on the point in literature that one scarcely knew what was meant by the term. Thus one could not judge properly of the results of operation in a large number of cases. He thought such terms as Graves's disease and Basedow's disease should be dropped. The term used largely in America, hyperthyroidism, was less open to objection, because possibly exophthalmos was one of the late symptoms. The symptoms of this disease were very protean, and not necessarily present in every case, just as the Argyll-Robertson pupil was not present in every case of tabes dorsalis. Their medical friends must now concede that the operative mortality in goitre cases has been so reduced that cases might reasonably be operated upon at an earlier period than formerly. At the

celebrated Mayo clinic at Rochester, U.S.A., the mortality in operations for exophthalmic goitre has been reduced to 3.9 per cent. He did not think sufficient importance was usually attached to the preparatory treatment. The practice of the Mayos had shown that the application of X-rays to the tumour for some weeks before operation, and absolute rest in bed, with the administration of belladonna, were very important as aids to success. He was not satisfied unless he had the patient in hospital for at least three or four weeks, during which X-rays were applied every two days, and the patient was having considerable doses of belladonna. When he said rest, he meant such absolute rest as was insisted upon in tuberculous cases at Frimley, when the patient was not allowed to feed herself, to sit up in bed, to read the paper, or to see friends.

He feared there was a habit of using the term "cured" in a loose and unscientific fashion. Dr. Dunhill said that if a patient returned to work he was considered cured, but he (the speaker) did not regard that as a legitimate use of the term. A patient might have intestinal obstruction from carcinoma of the rectum, for which colostomy was done, and he could return to work, but no one would contend that he was cured. He thought the term should be restricted in the present connexion to patients in whom all the symptoms of the disease had disappeared as a result of the operation. He would like to know whether any Fellow had seen a case which had definite and marked exophthalmos in which the exophthalmos had entirely disappeared after the operation. He had seen many cases of marked exophthalmos which had been operated upon, and in not one of them had the exophthalmos entirely disappeared, although the other symptoms had greatly improved.

Mr. H. M. PAGE: Not having had experience in local analgesia in these cases I cannot form an opinion as to its merits in contradistinction to general anaesthesia, but I agree with the remarks on this point made by Dr. Scharlieb. I have given a general anaesthetic in twenty-five cases of Graves's disease. The first five were for tying thyroid vessels, the last twenty for the removal of a lobe or more. The first fourteen cases were given chloroform; seven of these by Junker's inhaler; one by sprinkling on lint. At the end of the operation the pulse was much hastened in all, in three, by my notes, reaching 180, 180 and 150 respectively. In the remaining six cases the Vernon Harcourt percentage inhaler was used. Morphia and atropine was given beforehand and oxygen given all the

time. One of these cases died and has been referred to by Mr. Armour. Two ended with a pulse of 150 and 180 respectively. I have used the Vernon Harcourt inhaler for several years and can say that the percentage used was very small, during much of the time only $\frac{1}{4}$ per cent., and occasionally none. Mr. Armour has described the moribund condition of the patient who died. I was asked to give a general anæsthetic after local analgesia had been tried and the operation begun. At the post-mortem an enormous thymus and much general enlargement of adenoid tissue was found. This was not a fair case to judge general anæsthesia by as there was time lost and interference with the patient by the attempt to operate under local analgesia, but I believe that the chloroform helped to cause death.

The last eleven cases of this series were given ether by the open method. All of them had had morphia and atropine or morphia and scopolamine previously, and oxygen was given continuously during the administration. These cases gave me no trouble whatever. There was no cyanosis or excessive bleeding, and this fact was confirmed by the surgeons who operated, though amongst them were cases with some stridor and histories of bad dyspepsia. The pulse and general condition of the patients were hardly altered at all, except in one case, where the bleeding was sufficient to exsanguinate the patient, the pulse in the temporal artery being lost. The hæmorrhage was sudden and profuse, and I can assert was not due to ether. As Mr. Armour was so kind as to say that I had given the anæsthetic to nearly all his cases I should like to say that he was not the operator. This case was practically all right the next day. I give a few instances of the conditions of the pulse at the end, after ether, from my notes:—

Before operation			After operation	
140	150
108	108
Fast	The same rate
120	100 (less)

As to vomiting, in some of the cases it was absent, never more than emptying of the stomach before complete return of consciousness, except in a case of chloroform anæsthesia in which the vomiting lasted twenty-four hours. In none of the cases was there any lung trouble or other sequelæ.

In view of my experience with ether and remembering that nearly every post-mortem in cases of immediate death whilst operating in Graves's disease has shown a condition indistinguishable from lymphatism, I personally shall not give chloroform in the future.

If one might be allowed to eliminate the case of death in this series for purposes of argument as to the results of general anæsthesia, there would here be twenty-four cases operated upon under general anæsthesia without a death.

Mr. BETHAM ROBINSON said he had hoped to hear somebody speak about that form of anæsthesia which, as it were, came midway between local and general anæsthesia—namely, the intravenous method. Recently, in a case of exophthalmic goitre, or rather a case of adenoma with exophthalmic symptoms, he had administered for him hedonal intravenously, and he was immensely struck with the perfect ease with which he was able to carry out the operation. The patient was as if asleep; there was no congestion or respiratory embarrassment, and the shelling-out of a large tumour, almost the size of his closed fist, was accomplished with practically no bleeding from the surface of the cavity. He did not believe he ligatured any vessel, and there was no trouble afterwards. The method seemed to promise very well, for he considered local anæsthesia was not satisfactory for these cases. Of general anæsthetics, he preferred open ether; he disliked chloroform for these cases, and he had a vivid recollection of a case of exophthalmic goitre under his own care whose death he felt was due to the administration of chloroform.

Mrs. DICKINSON BERRY regretted that more light had not been thrown on the question how far general anæsthesia, even when the anæsthetic is taken perfectly well, constitutes an additional risk in operations for exophthalmic goitre. She recalled two cases, operated on by different surgeons, to one chloroform was given, to the other open ether; in both the anæsthesia was light and quite satisfactory. Both patients were considerably collapsed at the end of the operation, and both died within thirty-six hours. In cases like these, might the result have been different if no general anæsthetic had been used? She had seen operations for ordinary goitre done under local anæsthesia, and was surprised to find how little pain seemed to be felt. The patients were told that at any time a general anæsthetic would be given if required, but none had asked for one. One patient gave as her chief complaint the disagreeable sensation of the blood trickling down.

The CHAIRMAN (Dr. W. J. McCardie) remarked that not much had been said in the discussion as to the association of status lymphaticus—so important from the anæsthetist's point of view—with the condition

of exophthalmic goitre. He was very glad to hear Mr. Page mention lymphatism. It was generally agreed that the thymus co-operated in causing exophthalmic goitre, and there was great reason to suppose that the size of that gland might be some indication of the extent or severity of the co-existent lymphatism. Garré recorded a case of excision of the thymus only in a case of what was termed "florid exophthalmic goitre." The goitre was not excised, but the patient was practically cured. Capelle and Bayer also recorded improvement after thymectomy in a case of exophthalmic goitre. Those cases showed the co-operation of the thymus. If the thymus was so generally enlarged and the heart constantly dilated, ether should be chosen, because it was less toxic than chloroform, if general anaesthesia was used. The too stimulating effect of ether on the respiration should be "damped down" by the preliminary administration of morphia and scopolamine. In opposition to the generally accepted theory of the co-operation of the thymus with the thyroid, Gebele concluded that the thymus hypertrophied compensatorily to do the work which the thyroid could not do. If that were so, it was so much the better for the patient and for the anaesthetist. With regard to the question of local versus general anaesthesia, he had seen several operations done under local anaesthesia, and the strain during the injection, if it were thorough and deeply cervical, was described afterwards as being as great as that of the operation. Dr. Dunhill and Dr. Kocher advocated local anaesthesia; Sir Victor Horsley thought the choice of an anaesthetic mattered little; the Mayos and Krecke saw no reason to abandon ether; Crile advocated what he called "anoci-association" with general anaesthesia. Therefore there was no general decision as to the choice of anaesthetic among those whose experience was greatest. Of course, with a general anaesthetic the psychic factor was abolished, and that was very important. Whether local or general anaesthesia were chosen, there should be a preliminary injection of scopolamine and morphia, as that abolished the psychic danger, and greatly diminished the toxicity of ether and chloroform by lightening the anaesthesia. The disadvantage of the preliminary injection was that it increased the venous oozing, and the surgeons sometimes complained that this seriously complicated their work. There could be little doubt that such drugs as atropine and hyoscine caused venous dilatation. In the worst cases of exophthalmic goitre he believed that even the slight toxic effect of a general anaesthetic should be avoided. The Society was much indebted to Mr. James Berry for arranging this most interesting discussion, which had extended over three whole evenings, and he would ask Mr. Berry to summarize it.

MR. JAMES BERRY: I am sure, Sir, that all will agree with me in regretting that Dr. Dunhill himself is not present to reply, and that the duty of winding up this most interesting debate should fall upon myself. The debate to which we have listened has been most valuable and instructive, and will help, I hope, to crystallize the ideas of some of us surgeons who have hitherto been uncertain as to the manner in which we should deal with these most difficult cases of Graves's disease.

I do not intend to weary you at this late hour of the evening with any detailed exposition of my own views, partly because, like Sir Victor Horsley, I have already given them at some length in the debate at the Hunterian Society two years ago,¹ and partly because among the operations that I have performed for the removal of goitre of various kinds (which now amount to over 670) the number of cases in which I have thought it right to operate for genuine Graves's disease has been small—namely, eleven only. Besides these eleven cases there were, of course, a large number of those so-called cases of Graves's disease with which everyone who operates much for goitre must be quite familiar—namely, cases of parenchymatous or adenomatous goitre, with rapid pulse, tremor, and other symptoms simulating those of true Graves's disease. Such cases are often included in the gross statistics of operation for Graves's disease, and I quite agree with Dr. Kocher in thinking that it is misleading to do so. These cases are extremely satisfactory for treatment by operation, as they are practically always completely cured, and there is little or no risk in operating upon them. I have never lost a case of this kind, although I have lost two cases of genuine Graves's disease—one ten years ago, after ligation of three thyroid arteries, the other recently after removal of three-quarters of the gland.

In the very great majority of the cases of *true* Graves's disease which have come under my notice I have declined to operate, as I have not considered that the benefits to be obtained justified the risks, except in rare and isolated instances. Even at the present time, when our knowledge of the technique has been greatly advanced by the labours of the Kochers in Switzerland, the Mayos in America, Dr. Dunhill in Australia, Mr. Edmunds, Mr. Leedham-Green, Mr. Trotter and others in this country, there is still much to be done before operating on Graves's disease can be considered really satisfactory. Anything like indiscriminate operating for Graves's disease is, in my opinion, strongly to be deprecated. In carefully selected cases much good may be done by judicious and carefully executed operation, but the idea that

¹ *Clin. Journ.*, 1909, xxxiv, pp. 268-72.

a case of Graves's disease has only to be operated upon to be forthwith cured (although a prevalent one in some quarters at the present day) is, I venture to think, a grave mistake.

It is a little difficult to reconcile the optimistic view of Dr. Dunhill with the actual results that are being obtained in this country by most of those who do from time to time operate for this disease. I can but congratulate Dr. Dunhill on the excellent results that he has been able to obtain, although at the same time, with Dr. Hector Mackenzie, I wish that he had indicated a little more clearly how many of his cases really come under the category of genuine Graves's disease.

With the view of ascertaining, if possible, the actual results that were being obtained in the various London hospitals I sent a form of inquiry to the Surgical Registrars, and I am exceedingly indebted to Messrs. Fenwick, Gauntlett, Kennedy, Webb, Bolton, Etherington-Smith, Williams and Farrant, the Surgical Registrars of the Charing Cross, King's College, London, Middlesex, Royal Free, St. Bartholomew's, St. George's, University College and the Westminster Hospitals for kindly supplying me with statistics of ninety-seven cases, which have occurred in these hospitals in the last few years. These cases, with very few exceptions, were all typical, well-marked examples of the disease.

The results appear to have been much the same at nearly all the hospitals (except at the Middlesex, from which ten cases have been reported with no deaths). The total number of deaths in these ninety-seven cases has been sixteen. Of the sixteen deaths at least twelve occurred within forty-eight hours of the operation, and most of these within twenty-four hours. These do not include Dr. Mackenzie's figures at St. Thomas's Hospital, which are no better than the average at other hospitals. Of the patients who survived, most are reported to have been benefited by the operation, some in a very remarkable manner. Of the ultimate results of the operation but little is known. In only ten of the ninety-seven cases is local anæsthesia reported to have been employed; in at least fifty-five chloroform was the anæsthetic employed; in most of the remainder ether was used in one form or another.

It is possible that the poor results that most of us in this country have obtained from our operations for Graves's disease have been due, as Dr. Kocher seems to indicate, from not operating early enough. On the other hand, it must be remembered that the prognosis in early cases is by no means wholly bad, and that many patients recover completely under medical treatment. Another point is the uncertainty of the prognosis; one of Professor Kocher's assistants told me: "You never

know quite where you are with this disease." I am inclined to think that if the disease, after several months of medical treatment, shows no signs of improvement, and at the same time the symptoms are not very acute, the question of operation may reasonably be entertained. So wretched and miserable are many of the patients that there seems to me to be much force in the arguments used by Mr. Trotter, that we should not dwell too much upon the mere mortality of the operation. If we can show that a considerable proportion of patients can really be cured or even greatly benefited by operation, it is worth while to run some risk, provided this risk can be kept within reasonable bounds.

The conclusions which I venture to submit to the Society are as follows :—

(1) That operations for true Graves's disease must always be regarded as serious and even dangerous—far more so than are operations for ordinary goitre.

(2) That the danger is greatest in acute cases, and also in advanced cases where secondary degeneration in the heart muscle and elsewhere has taken place.

(3) That the danger can be mitigated, to a certain extent at any rate, by the observance of certain strict precautions before, during, and after the operation. Before the operation preliminary treatment by rest in bed for some little time is highly desirable, in order to get the heart into as favourable condition as possible. During the operation, it need scarcely be said, scrupulous asepsis and exact hæmostasis are all important. Gentleness in manipulation, and reasonable speed and dexterity in operating, are important. To insure these, it is desirable that not only the operator but also the assistant should have considerable experience of operations upon the neck.

(4) Considerable judgment must be exercised in determining the exact amount of gland tissue that is to be removed. In most cases, it seems to me, hemithyroidectomy should be the operation of choice. In very bad cases it is probably better to be content at first with ligature of one or both superior thyroid arteries. It should be remembered, however, that death may follow even this simple operation.

(5) After the operation, patients nearly always for a day or two show severe reaction; the pulse increases in frequency, the temperature may rise, there is often much excitability and restlessness. The administration of large amounts of fluid, whether by mouth or rectum or subcutaneous tissue, is perhaps the most important point in the after-treatment.

(6) It is in this latter respect, as Dr. Dunhill points out, that local

anæsthesia has a great advantage over general anæsthesia. The patient is able to drink large quantities of water immediately after the operation, and the danger of syncope is thereby greatly lessened. I confess to a strong feeling of preference for local anæsthesia for exophthalmic goitre (although not, as a rule, for ordinary goitre). If a general anæsthetic must be employed, and in many cases it must be, then the balance of evidence appears to me to be strongly in favour of ether administered by the open method. I cannot help believing, in spite of what has been urged to the contrary by some speakers, that chloroform, however skilfully administered, does add materially to the risks of the operation, and personally I should never now employ it.

(7) With regard to the ultimate results of the operation, I do not think that the evidence is at present sufficiently strong to enable us to express a decided opinion. It is greatly to be desired that those who operate much for Graves's disease should publish, not merely gross statistics with mere percentages of deaths and cures, but *detailed* lists of consecutive cases, stating clearly the condition of each patient both before and some considerable time after operation in each case. Until this is done—and so far as I know it has never yet been done on any large scale—we shall never arrive at any really satisfactory conclusion as to the desirability or otherwise of operating for Graves's disease.

Mr. Berry added, in connexion with a patient, a clergyman, aged 37, whom he showed, that, unlike the patient whom he exhibited at the meeting last week (whose case was a very acute one, and required many weeks of treatment before operation could be safely attempted), the present patient was an instance of moderately severe, rather chronic, Graves's disease. The disease had been in existence eighteen months. In July last this patient had been seen in consultation with Dr. Dunhill, who strongly urged Mr. Berry to operate upon him, giving as one of the reasons that he already had some œdema of the feet. There was then considerable exophthalmos, and the pulse ranged from 110 to 120. The operation had been done on the lines which Dr. Dunhill recommended, and under local analgesia—namely, novocain. Most of the right lobe and two-thirds of the left lobe of the thyroid were removed. He showed the patient now as an example of what might be regarded as an ordinary result seven or eight months after an operation for Graves's disease. There was still slight exophthalmos, the pulse was usually now 80 or 90, but when the patient was excited it became a little quicker. He felt much better than before, and could now do things which previously he could not, but it could not be said that he was yet cured.

Surgical Section.

March 12, 1912.

Mr. CLINTON T. DENT, President of the Section, in the Chair.

Case of Pancreatic Calculus; Stone removed by Operation.

By JOHN MURRAY, F.R.C.S.

CASES of pancreatic calculus are undoubtedly rare, and so few operations for the removal of a pancreatic stone have been recorded that I venture to bring the following case before this Section:—

The patient was a female, aged 40, whom I saw in consultation with Dr. Edwards, of Harrow, in September, 1910. She stated that she had suffered from anæmia when young, and had been liable to headaches from her earliest recollections. At the age of 18 (1888) she first began to suffer from attacks of pain in the epigastrium. The attacks used to come on immediately after food, the onset was sudden, and the pain so severe that the patient had to be carried upstairs and put to bed. The pain usually lasted about two hours and was not accompanied by vomiting. After the pain subsided the patient felt quite well. These symptoms continued for seven or eight years; after that time the attacks became less frequent, in fact, for a period of two years she was free from pain. Then the attacks of pain recurred, similar in nature, but more frequent. Sometimes there would be two attacks in a day, while at other times the pain would recur every day for a week. About ten years ago she had a severe attack which lasted eighteen hours, and was accompanied by jaundice. The patient stated that after a bad attack of pain she used to pass a large quantity of dark blood *per rectum*, and often felt faint.

The following notes have been kindly furnished by Dr. Edwards who was first called to see patient in November, 1899, about midnight.

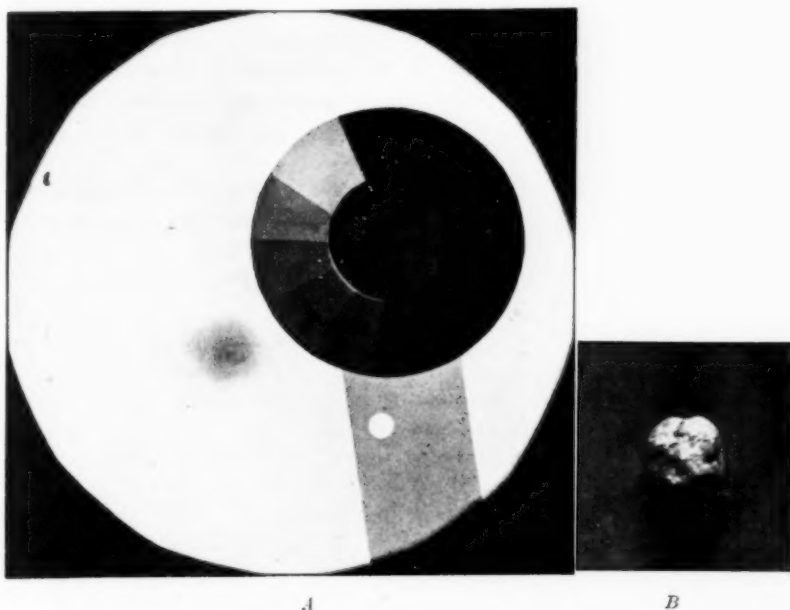
He found her suffering from severe epigastric pain and tenderness, for the relief of which morphia had to be administered hypodermically. The pain continued off and on for a fortnight. There was no jaundice, but he regarded the symptoms as "unequivocal of a stone in the cystic duct." He attended her from time to time for similar attacks, and in 1903 noticed that there was cardiac irregularity associated with gastric dilatation. In 1905 she suffered from occasional slight colic, more or less persistent pain referred to the right costal margin and epigastric tenderness. In 1906 Dr. Edwards noted vomiting, epigastric tenderness, and cardiac irregularity. During 1907 most of the attacks were accompanied by vomiting. From 1907 until July, 1910, the patient was much better, though still suffering from constantly recurring pain and discomfort, always referred to the epigastrium and right hypochondrium. On July 23, 1910, she had severe colic accompanied by vomiting, and she became jaundiced. Dr. Edwards concluded that the stone had reached the common bile-duct, and urged operation, as he had already frequently done, but the patient refused. The jaundice continued until the middle of September, with occasional attacks of pain and sickness, when she consented to submit to operation. She was then deeply jaundiced, the gall-bladder was distinctly enlarged, and could be easily felt extending 2 in. below the costal margin. As the symptoms seemed to point so clearly to the presence of gall-stones there is no information as to the nature of the stools, or as to the condition of the urine.

On September 24, 1910, the abdomen was opened by a vertical incision through the right rectus. The gall-bladder was distended. This was aspirated, and several ounces of bile drawn off. There were no stones in the gall-bladder, but on examining the bile-ducts with the finger in the foramen of Winslow a stone was felt which was thought to be lodged in the common duct. It was fixed with the left forefinger and thumb, but as the duodenum was obviously covering the stone I decided to enlarge the incision in the abdominal wall so as to render it more accessible. After doing this I failed to find the stone, although the common bile-duct, stomach, duodenum, and upper part of the jejunum were carefully examined. It did not occur to me that the stone might be in the pancreatic duct. Hoping that the stone had been pushed into the duodenum, I decided to close the abdomen, inserting a tube into the gall-bladder. The recovery was uneventful, the jaundice rapidly disappeared, and the wound healed.

At the end of six weeks the patient returned home, and the same

day she was suddenly seized with pain and vomiting, and very soon became jaundiced. The attack lasted twenty-two hours. The gall-bladder became distended, and subsequently the scar broke down and a large quantity of bile escaped. The jaundice subsided, and bile continued to drain from the gall-bladder.

On November 7 the abdomen was re-opened and the gall-bladder separated from the parietal peritoneum. The stone was at once felt in its original situation, lying behind the second part of the duodenum.



A, skiagram of stone showing greater density of nucleus, compared with Benoist's scale; *B*, photograph of pancreatic stone (natural size).

It was fixed with left forefinger and thumb, and the peritoneum divided on the outer side of the duodenum. The duodenum was raised up and displaced towards the left side. After carefully tearing through some pancreatic tissue the duct was exposed, and an incision made in the wall through which the stone was easily removed, when some clear fluid, obviously pancreatic fluid, escaped. The opening in the duct was closed by three fine silk sutures. Two drainage-tubes were

introduced, one into gall-bladder, and one towards the outer edge of the duodenum. The gall-bladder was sutured to the parietal peritoneum, and the abdominal wound closed.

The patient made an uninterrupted recovery and there was no leaking from the sutured duct. I have lately seen the patient: she is in good health, and has had no pain since the second operation. The stone is globular, grey in colour, irregular on the surface and measures 12 mm. in diameter.

Composition of the Stone.—Dr. Kellas, who has kindly examined the stone, writes: "I have investigated the pancreatic calculus left with me and find that the outside of it consists of fairly pure cholesterol with a trace of an iron compound. There may be a trace of fat present as well." The interior has not been examined, but the skiagram shows that it contains a nucleus more resistant to X-rays than the exterior.

The symptoms in this case are similar to those noted in the previous cases recorded—viz., colic, simulating gall-stone colic, only less severe in character, unattended by jaundice, occasional sickness, and epigastric pain. The right-sided nature of the pain in this case was distinctly misleading.

It must have been the misfortune of most surgeons to undertake an operation for gall-stones and, on opening the abdomen, find the gall-bladder devoid of calculi. Had this stone not been fixed in the ampulla I do not expect it would have been detected. In such cases it is well to bear in mind the possibility of the presence of a pancreatic stone, and the close resemblance between the symptoms caused by pancreatic calculi and gall-stones.

Operations for removal of pancreatic calculi have been recorded in this country by Sir Alfred Pearce Gould, Mr. Moynihan, and Mr. Mayo Robson. In Sir Alfred Pearce Gould's case¹ several stones were removed from the duct of Wirsung by an incision through the head of the pancreas. Mr. Moynihan² diagnosed and removed a stone through the duodenum and Mr. Mayo Robson³ removed four stones, one from the duct of Wirsung, one from the duct of Santorini, by incisions in the head of the pancreas, and two through the duodenum.

Mr. Mayo Robson, in his Hunterian Lectures, mentions the method I adopted in this case as a possible route by which to reach

¹ *Trans. Clin. Soc. Lond.*, 1899, xxxii, pp. 59-63.

² *Lancet*, 1902, ii, p. 355.

³ *Lancet*, 1904, i, p. 913.

a pancreatic stone, but I have not been able to find a similar operation recorded, and it appears to me that where the calculus is lodged near the ampulla, it is preferable to remove the stone by separating the duodenum, and displacing it to the left rather than by an incision in the anterior wall of the duodenum.

DISCUSSION.

The PRESIDENT (Mr. Clinton T. Dent) remarked that such cases were rare, and it would be very interesting if any Fellow who had had experience of such, either on the operating table or in the post-mortem room, would relate it.

Dr. P. J. CAMMIDGE agreed that cases of pancreatic calculi were very rare. Oser, when he wrote the article on the Pancreas in Nothnagel's "Encyclopædia of Medicine," in 1903, found seventy cases recorded, and probably the total number of cases reported to date did not exceed eighty. In the cases which Mr. Murray mentioned as having occurred under the care of Mr. Moynihan and Mr. Mayo Robson, he (the speaker) had the opportunity of examining the fæces and urine of both. In each case the urine gave a well-marked pancreatic reaction, and contained large numbers of calcium oxalate crystals. The fæces also showed evidence of marked pancreatic insufficiency, and those two points taken together helped to confirm the diagnosis of pancreatic calculus. The chief difficulty was to differentiate a pancreatic calculus from one in the common bile-duct. If a pancreatic calculus lodged in the ampulla of Vater, as it had in this case, and had apparently been there for a considerable time—for it was covered with a shell of cholesterin—the diagnosis, he contended, was practically impossible to make, by chemical means at any rate, although it was likely that if a skiagram had been taken at the time some suggestion might have been made as to it being denser than ordinary gall-stone. Still, when a stone was lodged in the lower part of the common bile-duct there were symptoms by which it could be distinguished from a stone which was only present in the pancreatic duct. One of the most important, in his experience, was that when there was a stone floating or only partly impacted in the common duct there was nearly always an exceedingly well marked reaction on testing for urobilin in the urine. In two cases where he had examined the urine for pancreatic calculi there was no urobilin at all. This might be a useful point to remember in making a diagnosis. Another point that might help in the diagnosis was the examination of the stools. All experimental evidence tended to show that pancreatic calculi were formed as the result of inflammatory changes in the pancreas, causing collections of material on which lime salts crystallized out, and that being so, one usually found that

a person who had a pancreatic calculus had his pancreas rather extensively fibrosed, and therefore the digestive fluids of the pancreas poured into the intestine were defective. On examining the faeces in such a case of sclerosis of the pancreas, one found an excess in total fats, and the greater part of these fats was usually unsaponified—i.e., it had not been digested. If there was a gall-stone in the common bile-duct, and there was not advanced sclerosis of the pancreas, then, although there was an excess of fat in the stools, yet when one separated it out, the excess of fat in that case consisted of saponified fat, because the pancreatic juice had digested the fat, but the fat had not been absorbed because the bile which was necessary for its complete absorption had been defective in amount. Another reason was, probably, that gall-stones were, after all, only a secondary result of a chronic intestinal catarrh, and when that was present there was not as complete absorption as there should be, and there was an excess of saponified fat in the stool. Another point was that in several cases of pancreatic calculus described, irregularity of the heart's action had been noted. This was an interesting observation in connexion with the fact that in many cases of pancreatic cirrhosis a large amount of calcium salts was found in the urine, and it was known that the action of such salts upon the heart muscle was to produce a steadying of the beat.

Mr. BETHAM ROBINSON said that an important point surgically was the likeness between the present case and those in which a stone was present in the common bile-duct or in the ampulla of Vater. Those who had had experience of cases of calculus in the ampulla of Vater would agree as to the difficulty of diagnosis; in fact, if there were a stone in the ampulla of Vater which blocked the common duct and pancreatic duct it would, he thought, be impossible to say from which duct it had come. Again, there might be a pancreatic calculus which was in the terminal part of the duct of Wirsung and which, by pressure, blocked the common bile-duct. A point of clinical interest concerned the X-ray investigation. As there were more lime salts in pancreatic calculus, a shadow would be a useful guide. And still another point was, that if the calculus were of biliary origin the presumption would be that instead of having a dilated gall-bladder that viscus would be contracted, owing to the previous gall-bladder trouble. In the case related the gall-bladder was reported to be very dilated, which would be due to the pressure on the end of the common bile-duct from the pancreatic calculus or swollen head of the gland.

Multiple Tumours of the Large Intestine.

By G. H. MAKINS, C.B., F.R.C.S., CUTHBERT WALLACE, F.R.C.S.,
and PERCY SARGENT, F.R.C.S.

THE following cases have occurred in our practice in a comparatively short period of time. It is therefore probable that they are more frequent than the text-books would lead one to suppose. As they seem in addition to offer some food for reflection, both from a clinical and pathological point of view, we have thought it worth while to put them on record.

Case A.—T. C., a male, aged 39, suffered from colic and diarrhoea in October, 1903. The pain lasted on and off until Easter, 1904, when he again sought medical advice and was treated, but with indifferent success. In July, 1905, the patient saw Sir Lauder Brunton, who in November, 1905, advised operation. The patient at this time suffered from a gnawing pain between the umbilicus and pubis, which was independent of food but occurred both before and after defecation. The bowels were regular. Examination showed a definite mass the size of a tangerine orange just below and to the right of the umbilicus. November 15, 1905: A cœliotomy showed a massive nodular growth in the transverse colon and a smaller but similar growth 6 in. from it on the splenic side. There were glands near the bowel. The two masses with the glands necessitated the removal of 14 in. of the bowel. The divided ends of the bowel were united by end-to-end suture. There was a small temporary fœcal fistula, but with this exception union was good. The specimen showed two distinct growths of the transverse colon with a perfectly normal length of intestine between them. The upper one was the larger and encircled the bowel for some inches. Its surface was ulcerating. The lower growth was the smaller. The mucous membrane over it was intact. After the operation the patient had several attacks of colic and an indefinite mass was felt occasionally in the left iliac fossa; it was thought to be probably fœcal. The patient left the home on December 23, 1905. Dr. Dudgeon reported that the glands were infected with colloid carcinoma.

January 16, 1906: Patient reported that the colic continued at times, but an examination of the abdomen and rectum revealed nothing abnormal.

In January, 1908, the patient sought advice on account of chronic obstruction and a tumour in the left iliac fossa. On January 28 the abdomen was opened and a ring carcinoma the size of a hen's egg was found at the junction of the pelvic and iliac colons. There was no sign of dissemination. The

growth was removed and the bowel joined by an end-to-end anastomosis. With the exception of a small faecal fistula the recovery was uneventful.

In February, 1911, the patient reported himself as being in health and following his occupation as a clerk.

In May, 1911, the patient again presented himself with a mass beneath the right rectus near the original incision. Coeliotomy revealed an ulcerating ring carcinoma situated immediately on the caecal side of the line of the first resection. This line had apparently strictly limited its downward extension. The mass was excised and the small gut and transverse colon united by end-to-end suture. Recovery was uninterrupted.

In February, 1912, the patient came under treatment for the last time suffering from a ring carcinoma of the rectum. The growth was situated 4 in. from the anus and reached up for another 3 in. A colostomy was performed in the inguinal region, and an examination of the abdomen showed that the liver was unaffected and that there was no peritoneal infection. The rectum was excised by the para-sacral route. There were three small infected glands in the meso-rectum. The patient did not survive the operation. No post-mortem examination was allowed. The interval between the first and last operation was six years and two months.

Case B.—T., female, aged 53, a patient of Dr. H. Simpson, of Brenchley. A severe attack of constipation occurred in June, 1908. At this time some swelling in the left iliac fossa was noted but no other physical signs. In September another attack occurred which only partly yielded to treatment. An examination of rectum proved negative. In October, 1908, the difficulty with the bowels increased in severity until a period of eight days' complete constipation supervened and castor oil and enemata only produced mucus. A rectal examination now showed a growth just within reach of the finger and still covered by mucous membrane. There was a resistance in the left fossa but no definite tumour. The abdomen was opened and a contracting ring carcinoma found at the middle of the sigmoid loop. The presence of the growth felt *per rectum* was confirmed by a hand in the pelvis. It was on a level with the cervix uteri and movable. There was fluid in the belly but no secondary growths. The colon both above and below the sigmoid growth was hypertrophied. The sigmoid growth was excised and a colostomy established. The excision of the lower growth would have entailed a dangerous operation for which consent had not been given. The patient elected to go home with the colostomy opening and she left the home much improved. She died with a local recurrence or extension in December, 1910. The growth was microscopically columnar carcinoma.

Case C.—A male, aged 56, was admitted to St. Thomas's Hospital with intestinal obstruction. A colostomy was performed, but death ensued. At the post-mortem examination the whole of the large intestine was beset with polypi. There were two ulcerating cancerous strictures separated by 8 in.

of normal bowel. The higher of the two carcinomata was 12 in. from the cæcum. (Specimen No. 1131A, St. Thomas's Hospital Museum.)

Case D.—E. R., female, aged 43, was admitted to St. Thomas's Hospital in 1907. She gave a history of attacks of vomiting and diarrhœa lasting over seven years and of obstruction for fourteen days. Rectal examination showed a large hard growth, just within reach of the finger, by which it could be pulled down for some distance. A transverse colostomy was performed. Sixteen days later a perineal excision of the rectal growth was attempted, it being judged that the operation would prove easy on account of the mobility of the growth. The mass was easily reached and mobilized, but when the bowel was cut across above the growth, although the muscular wall was normal, the condition of the mucous membrane was rough, uneven, and suggested an extension upwards of the growth. More bowel was therefore freed and about 12 in. brought down outside the anus. The appearance of the mucous membrane was still abnormal, but the condition of the patient necessitated the finishing of the operation. The bowel was therefore cut across and sewn to the anus. The patient died in twenty-six hours. The resected portion of intestine showed an ulcerating stricture 4 in. from the anus. The mucous membrane between the growth and the internal sphincter was covered with small shaggy papillomata. The bowel at the point of section was similarly affected. At the post-mortem examination the following conditions were found. The transverse colon was hypertrophied. At the splenic flexure was a dense ringlike stricture greatly reducing the lumen of the bowel. The mucosa below the stricture and down to the point of section at the operation was thickened, rugose, and studded with multiple polypoid sessile growths. There was no ulceration of the mucosa, nor were there any secondary deposits. Microscopically both the ring growth at the splenic flexure and also the ulcerating growth in the rectum proved to be columnar carcinoma. The polypoid growths in the colon were benign.

Case E.—Female, aged 66, gave a history of one year's pain and constipation. There was a nodular fixed tumour in the right iliac fossa. Cæliotomy showed a tumour involving 4 in. of the ascending colon, and increased towards the mid-line by a mass of glands. The transverse colon was divided 3 in. from the hepatic flexure and the right colic artery tied. The colon and upper 6 in. of the ileum with the peritoneum and enclosed glands were removed. The ileum and colon were joined by a lateral anastomosis. Six weeks after operation the patient was seized with sudden pain, and an abdominal tumour suggesting a twisted ovarian appeared. She was tapped and bloody fluid drawn off. A hard nodular mass was then left in the pelvis. The patient died three months later. On opening the colon a number of polypoid growths were found on the distal side of the colon. No microscopic examination was made.

Case H.—C. W. S., aged 32, grocer, was admitted in January, 1910, with a six months' history of two attacks of diarrhœa and passage of bright blood *per*

rectum. There was a hard mobile tumour in the left iliac fossa and a pedunculated tumour on the posterior rectal wall. The rectal polyp was removed, and proved microscopically to be an adenoma. In March, 1910, patient was again admitted with a month's history of two attacks of colic, accompanied with pain in the abdominal tumour. December, 1910: Eight inches of iliac and pelvic colon were resected, towards the top of which was an annular growth partially obstructing the lumen. A colostomy was established. The mucous membrane of the resected portion showed multiple masses of polypi below the annular growth with definite clinically malignant ulcers between them and many minute polypi above the growth up to the point of section. The annular growth was microscopically a columnar-celled carcinoma; the polypi were microscopically complex adenomata; the clinically malignant ulcers were columnar-celled carcinomata.

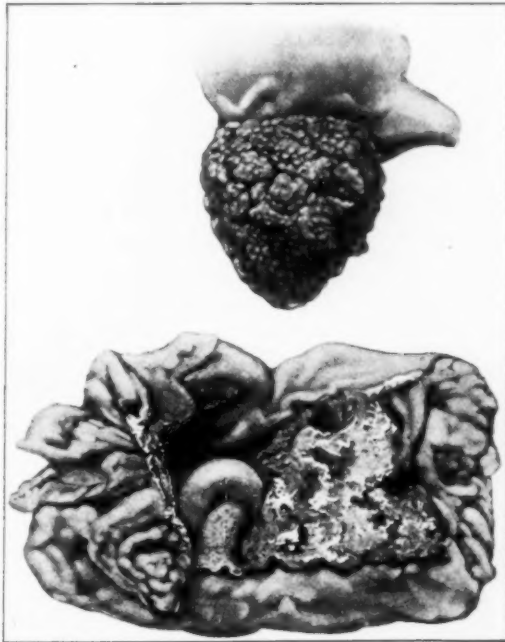
Case J.—Female, aged 34, gave a history of twelve months' constipation. The transverse colon was divided and the hepatic flexure, the ascending colon containing the growth, the cæcum, and some 3 in. of ileum with the overlying peritoneum and glands on the right colic arteries were removed. The ileum and colon were joined by lateral anastomosis. The colon when opened disclosed an annular stricture at the commencement of the ascending colon and below it a number of polypoid growths were scattered, at gradually increasing intervals, as far as the hepatic flexure. Microscopically, both the main growth, the polypoid masses, and the glands presented the typical appearance of columnar-celled carcinoma. The patient was well in March, 1912.

Case K.—A lady, aged 51, a case of Dr. Spurrier's, of Maidenhead, gave a history of attacks of constipation, accompanied by slight obstructive symptoms, lasting for several months. In the last attack the treatment by enemata, which had previously been successful, failed to give relief, and although the general symptoms were slight, the abdomen gradually became more distended, and operation was advised. The transverse colon was very distended and showed peristalsis, stopping at the splenic region, the then probable site of obstruction. Whilst the patient was being assisted to put on some clothes, preparatory to being moved into a home, there was a sudden feeling of relief, followed by passage of flatus and large loose stool, and marked diminution in the size of the abdomen. It was now possible to feel a movable tumour in the splenic region, as well as the somewhat distended transverse colon running towards it. On opening the abdomen the tumour was found to be a ring carcinoma near the splenic end of the transverse colon, and, immediately proximal to it, another pedunculated tumour within the lumen of the bowel. The whole was resected and end-to-end junction effected. Microscopically, the stricture was a columnar carcinoma, and the pedunculated tumour was an adenoma (*see figure*). It was clear that the adenoma had become impacted into the stricture, and that the movements of getting up and dressing had effected its release. Unfortunately the patient did not survive the operation.

The cases seem to fall into four classes :—

(I) Ring carcinoma with a length of normal bowel between them—Cases A and B.

(II) Ring carcinomata having the mucous membrane of an otherwise normal bowel between them covered with simple polypi—Cases C and D.



Multiple growths of the great gut. The tumours described in Case K. The upper is the proximal adenoma which became impacted in the distal ring. Carcinoma depicted by the lower drawing.

(III) A ring carcinoma having the mucous membrane distal to it covered with (1) simple polypi—Case E; (2) simple and malignant polypi—Case H; (3) malignant polypi—Case J.

(IV) A ring carcinoma having a single simple polypoid adenoma just proximal to it—Case K.

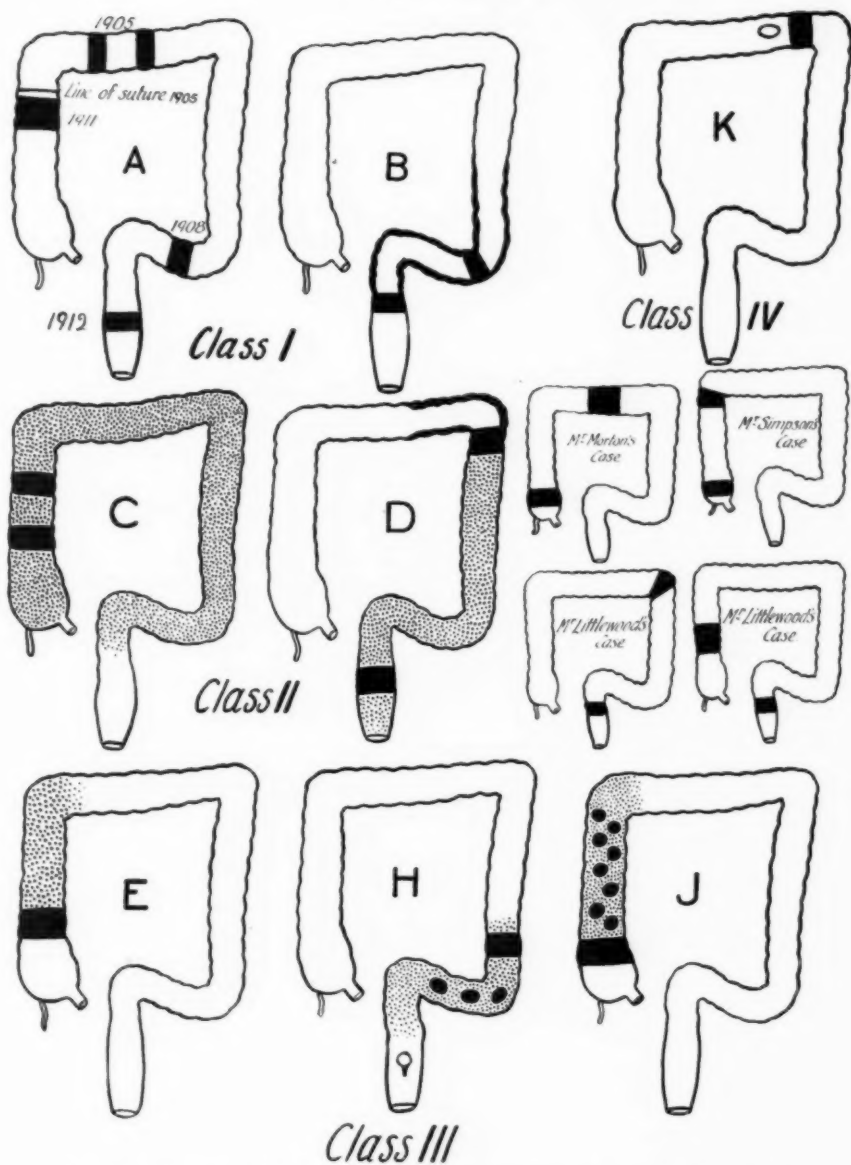
The questions at once occur: (1) What is the relation that these various growths bear to one another? (2) If one is secondary to

another, what is the method of dissemination? These questions cannot be fully answered, but there are some points that are of interest in this connexion.

Class I.—In this group there is no obvious way by which the infection might have been carried. It is quite true that proof is lacking that the infection did not travel by (a) lymphatic infection, (b) permeation, (c) peritoneal dissemination; but the fact that Case A lived six years after the first resection, and that no dissemination has been seen at the different operations, seem to make these methods of infection improbable.¹ There remains an alternative. Either the growths were primary or the lower were implantation or infection tumours. In this connexion the age date of appearance of the individual tumours is of importance. While there can be little doubt that the transverse colon and sigmoid tumours in Case A were present when the patient first came under observation, the facts that the transverse colon tumours caused the most inconvenience, and that of these tumours the upper was the larger and extensively ulcerated, point to the proximal being the eldest tumour of the three.

In Case B the fact that the bowel was hypertrophied above the lower growth might be taken as indicating that the lower had existed before the upper growth, but consideration will show that the upper growth might have remained sufficiently patent to transmit matter which had some difficulty in passing the lower, and later formed obstruction. On the whole the clinical evidence is not against the proximal being the oldest growth, and this fact, in so far as it goes, allows of the infective theory. Beyond this it is impossible to go. Morton's case of a second tumour in the transverse colon five years after a resection of a cancerous cæcum is indecisive. It might be considered evidence that the second tumour had arisen *de novo* after the excision of the cæcum, but considering the extreme chronicity of such growths, the transverse colon growth might have been present at the first operation, and therefore possibly an infection growth.

¹ To the cases detailed above can be added the following, quoted by Lockhart Mummery in "Diseases of the Colon." C. Morton (*Brit. Med. Journ.*, 1904, ii, pp. 1149-51) describes a case in which the excision of a cancerous cæcum was followed in five years by a carcinoma of the transverse colon. Littlewood (*Lancet*, 1908, i, p. 105) describes two cases: one, a female, aged 52, with a cancer in the splenic flexure and the rectum; a second, a male, aged 69, with a cancer of the ascending colon and of the rectum. G. Simpson (*Brit. Med. Journ.*, 1907, ii, p. 1649) describes a case where there was a cancerous stricture of cæcum and hepatic flexure.



Multiple tumours of the large intestine. The broad black bands indicate the site of ring carcinomata. The fine dots show the situation of simple papillomata. The large dots show the position of malignant papillomata. The small circles represent simple pedunculated polypi. The thick outline shows where the muscular coat has undergone hypertrophy.

Class II.—The mucous membrane of the bowel between the carcinomata is covered with simple polypi. The actual cases present some differences. In Case C the whole of the great bowel was affected with polypi; in Case D the bowel was normal above the upper ring carcinoma. The Case C, from the fact that the whole large bowel was polypoid, might be an example of cancerous change occurring in two places among pre-existing polypi. Mummery, quoting Quince and Landel, points out that a polypoid condition of the bowel often ends in carcinoma. That both carcinoma were found in the upper part of the polypoid bowel is, however, noteworthy. Case D is different. There were here two carcinomata. The upper was of the contracting ring type, and the muscle wall was hypertrophied above and not below it. It was therefore, presumably, the elder of the two carcinomata, the ulceration of the lower carcinoma being due to its type and situation. It is possible that the upper carcinoma caused the polypoid condition below it, and that the rectal growth was a cancerous transformation in the polypi so produced. If the possibility of this is admitted, can the last case be a similar one, the polypi above the proximal stricture being produced by an upward current. We are inclined to think not, as here the carcinomata were of the ulcerating, non-contractile type, such as found in the rectum in Case D.

Class III certainly seems to support the suggestion thrown out in considering Case D, that the upper carcinoma is responsible for the polypi below it. In this class there are two cases in which the bowel is completely normal above the ring carcinoma, and one in which it is only affected to a very slight extent above, while below it is grossly diseased. In Case E there is a ring carcinoma in the ascending colon, and the membrane of the bowel distal to it is covered with polypi at increasing intervals. In Case H there is a ring carcinoma of the iliac colon with the mucous membrane of the bowel distal to the growth beset with simple and malignant polypi. In Case J there is a ring carcinoma in the ascending colon, with the mucous membrane of the bowel distal to the growth beset with malignant polypi. It certainly is difficult to look at the diagrams of these cases and come to any other conclusion than that the upper ring carcinoma is responsible for polypoid condition of the bowel, and also, therefore, indirectly, for secondary carcinomatous change. How, otherwise, are we to account for the fact that the ring carcinoma in both Class II and Class III is actually at the summit or near the summit of the affected bowel. In Case E the polypi become set on the bowel at increasing intervals until they cease. This

decrease in the number of polypi, as the distance from the ring carcinoma increases, is in favour of our suggestion, since a waning influence of the carcinoma on the mucous membrane would be expected if our assumption is correct.

Class IV seems somewhat apart from the other cases, as the simple growth is situated on the proximal side of the carcinoma. It is possible that the mucous membrane, constantly forced against the cancerous surface by the peristaltic wave, was irritated to produce an adenoma. A more simple explanation, perhaps, would be that of two polypi one had become malignant.

The means by which the cancerous growth could have given rise to a polypoid condition of the distal mucous membrane is a matter of conjecture. The so-called contact carcinomata are well known.

There has lately been presented to the Museum of the Royal College of Surgeons, by Dr. F. J. McCann, a specimen (No. 4690C, Royal College of Surgeons Museum) which shows an ulcerating epithelioma of one labium vulvæ, and on the corresponding parts of the other labium a papilloma apparently produced by contact or irritation. Hurry Fenwick has also called attention to the fact that carcinomata of the bladder are able, by contact, to bring about the growth of papillomata. Is it possible that actual fragments, detached from the carcinomata, irritate the mucous membrane to produce polypi, or that the carcinomata excrete some toxin which has a similar effect?

There are also in this series one or two interesting clinical points. Case A shows how painless, chronic and slow to disseminate is carcinoma of the colon, and yet how persistent it may be in its local appearance. This knowledge certainly should influence the surgeon when he has to decide between the safe but palliative short-circuiting and the more dangerous radical operation. Cases A, B, D warn the surgeon that he must be prepared to find in the colon more than one growth. When the abdomen is opened for obstruction and a ring carcinoma is found, one is apt to take it that the excision of the growth found, provided there is no general dissemination, will remove the trouble. Littlewood has reported two cases which bear on this point. In one a colotomy failed to give relief for obstruction, caused apparently by a rectal carcinoma, and another where excision of rectum was followed in three months by obstruction caused by carcinoma in the ascending colon. It is well, therefore, in all cases of carcinoma of the great gut to make

sure by a careful exploration from cæcum to anus that no second cancerous stricture exists. A large carcinomatous mass or a general dissemination is not likely to escape, but a constricting ring carcinoma can easily be overlooked in the more or less cursory examination that one is inclined to make when the apparently offending stricture is held in the hand.

DISCUSSION.

Mr. PERCY SARGENT desired to add, in reference to Case A, that when the paper was written the patient was still alive and apparently in perfect health; but he returned a month ago with carcinoma of the rectum, that being the fourth cancerous growth of the large bowel from which he had suffered. It was a ring carcinoma of the ordinary type, and its removal by the trans-sacral route unfortunately proved fatal.

Mr. G. H. MAKINS, C.B., said he would have spoken of Case H as one of multiple polyposis of the large intestine, in which malignant disease had developed secondarily. If that were the case it might perhaps be the same with some of the growths which were situated higher up. Multiple polyposis in connexion with malignant disease was a very peculiar condition. It occurred in patients who, for carcinoma, were comparatively young, and such cases often only applied for advice when they had got obstruction. Occasionally one saw cases with polypi in the rectum, which on removal were found to be adenomata; but in that class of case the patient often returned with a definitely malignant growth, and one could not be certain whether the original polypi might not have been secondary to growth already existing. It was well known what a long time malignant growth in the large bowel might exist before giving rise to symptoms which materially affected the patient; and Mr. Cuthbert Wallace's paper raised the question whether the majority of cases so-called multiple polyposis, which were supposed to become secondarily malignant, might not be cases of malignant disease from the commencement. With regard to the series of cases recorded in the paper, the patient H was still alive, and patient J was in excellent health; there had been no sign up to the present of recurrence in her, nor, as far as he was aware, in patient H. In both, as far as he could tell, the bowel was clear of polypi beyond the point at which it was removed. Another point of interest which seemed worthy of mention was the difficulty sometimes experienced in deciding, after the performance of colostomy, whether failure of the anus to act was due to a second growth, or whether the patient suffered from atony of the bowel which prevented it working. That had exercised his mind strongly at times, and as Mr. Cuthbert Wallace had shown that these multiple growths were more common than had been supposed, such exercise of mind was not likely to be diminished. One case which he had

had strongly impressed that point upon him. The patient was brought to hospital with obstruction due to a sigmoid carcinoma, for which ordinary inguinal colostomy was performed, but the bowel refused to work, and the man was practically dying. While he (Mr. Makins) was away the resident assistant surgeon kindly did a right cæcostomy, and the man recovered. The patient remained in hospital till his death, and it was thought there must be multiple growths. The bowels were relieved by the cæcal anus, and although the inguinal anus remained open very little came out of it. At the post-mortem examination no secondary growth was found above, the colon had simply struck work and did not resume it after the attack of obstruction, and the belief that a secondary growth would be found between the two anuses proved incorrect.

Mr. GORDON WATSON remarked that he had seen one or two interesting cases in this connexion. With regard to multiple polypi in the young, last year he assisted Sir Frederick Wallis to operate on a boy aged about 8, who had multiple polypi of the rectum and troublesome prolapse with hæmorrhage; in fact, the whole of the lower 8 or 9 in. of the bowel was studded with innocent multiple polypi. The patient had no carcinoma above the growth, and he had remained well since the operation. He had twice done post-mortem examinations on cases of multiple polypi of the large intestine in which no evidence of malignant disease was found. So this condition could exist independently of malignant disease, although he felt certain that it was very often pre-malignant. In 1907 he operated upon a sergeant in the Police Force, whom he diagnosed to have polypi of the sigmoid owing to what he saw with the sigmoidoscope. The man also had a constricting carcinoma in the centre of his sigmoid. He resected the sigmoid with the carcinoma in the centre. There were a number of innocent polypi on each side. The patient did very well, remained in the Force, and was able to qualify for his pension. He died last year, four and a half years after the resection of the intestine. Post mortem the whole of his large intestine was found to be studded with multiple polypi. Three months before the patient died he examined the bowel with the sigmoidoscope, and the man had no polypi below the line of anastomosis. Thus those polypi which were below the anastomosis had appeared since that examination. This was suggestive of polypi being both primarily pre-malignant—i.e., precursors of malignant disease—and also secondary to malignant disease somewhere above. Another case, also of some interest in this connexion, was one at St. Mark's Hospital in 1908. It was that of an old gentleman from Herefordshire who had a large polypus in his rectum, which he (the speaker) removed, and the patient returned home. A year afterwards he came again with an inoperable carcinoma of the rectum. For that he did inguinal colostomy, and while the patient was in the hospital he developed intestinal obstruction. The house surgeon examined the colostomy wound with his finger, and found another growth above the colostomy. He (Mr. Watson) opened the abdomen, and confirmed the presence of the growth, which was in the descending colon and fixed. He therefore did a transverse colostomy. Neither at the time that he did the iliac colostomy

nor when he did the transverse colostomy did he see evidence of polypi or adenomata. But the patient had two independent carcinomata, and at the first operation he had an innocent polypus in the rectum.

MR. BETHAM ROBINSON desired to mention a case which had a bearing on the paper. The patient was in St. Thomas's Hospital thirty years ago, and was a young girl, aged 19, who came on account of obstruction. When she was operated upon it was found that she had in her pelvic colon a growth, and below that growth were numerous polypi. The question as to whether the polypi below were primarily non-malignant, or whether they were malignant from the first, he thought he could solve in regard to this particular case, because he took some of the polypi which were below the growth, examined them histologically, and found them to show evidence of malignant disease.

MR. CHARTERS SYMONDS said two points arose out of the admirable series of cases comprised in the paper. The question of multiple polypi had interested him for some time, and in some lectures which he gave at the Medical Society he related cases of polypi associated with cylindrical carcinomata of the bowel, and showed specimens of them. His cases were limited to those of primary disease of the caecum and first part of the ascending colon. In some of the cases the bowel for some distance was studded with large polypi. Those which he submitted to microscopical examination were non-malignant. He believed it was the general experience that in most of these cases of malignant annular strictures polypi were absent; and that rather confirmed the view that these polypi were primary, and therefore preceded the growth, although he had generally looked upon them as secondary to the growth. When one contrasted the absence of these polypi in the majority of cases of malignant growths in the large intestine, the inference was that they had preceded the development of carcinoma. Yet, on the other hand, it was curious that one should not find some symptoms indicating the presence of such polypi, as, for instance, hæmorrhage. The only good example he had seen confirmatory of these interesting cases of multiple stricture was that of a man who had a large carcinoma of the rectum, fixed to the pelvis, and in which a colostomy did not give relief. He was summoned to the patient later because he had intestinal obstruction. Nothing was done, but a large mass could be felt in the hepatic flexure. He was interested in the question of the mode of origin. He thought the suggestion made by Mr. Cuthbert Wallace that cases like Case B were implantation growths was likely to be correct, and that they corresponded with the multiple malignant disease found in the upper part of the alimentary tract, for instance, in the tongue and œsophagus, and in the palate and œsophagus, of which he had seen several examples. Interesting remarks had been made with regard to polypi generally, and Mr. Gordon Watson's case of multiple polypi of the rectum in a child especially interested him. A boy, aged 5, with multiple polypi of the rectum, was under his (Mr. Symonds's) care in the Evelina Hospital for Children many years ago. The polypi were so numerous, the surface was so studded with buttons of growth, that it was hopeless to

attempt removal. He took one out for examination, and left the others. He followed the case up, and four or five years later got an opportunity of examining the boy, and then found that the rectum was quite free from polypi. The case well illustrated the spontaneous disappearance of the polypi. He did not wish to generalize, but the case suggested that operation on this type was unnecessary. The boy had no treatment whatever. He believed there was another explanation of the type of case recorded by Mr. Gordon Watson in the Herefordshire patient. One might find in the rectum a polypoid growth over a large area, perhaps $1\frac{1}{2}$ in. in diameter, a growth which could be pulled outside the rectum and removed, and apparently freely removed, a growth which secreted an enormous quantity of mucus, so that the subject of it would pass 30 oz. of slight odourless clear mucus in a night. A small piece of such a growth might not show malignancy, but in every case in the end the patients had had malignant disease. And he thought that if the microscopical examination had been more thorough, some part would have been found to be malignant even at the time of removal. The important inference seemed to him to be that if in resecting these cases multiple polypi were found, it seemed to be right to go beyond any of these growths in the operation. He would like to hear Mr. Cuthbert Wallace's opinion on that point.

Mr. CUTHBERT WALLACE, in reply, said that though he had not laid stress on it in the paper, there were two kinds of carcinoma. Both growths in the Case C and the lower growth in the Case D were of the superficial ulcerating type involving only the mucous membrane of the bowel. They arose from a malignant change in the pre-existing polypi. The other carcinomata were of the ordinary contractile type involving all the coats; they were primary growths, whereas the ulcerating tumours were secondary. He agreed with Mr. Charters Symonds that a clean sweep of the polypi was advisable.

Hydrocephalus Internus; Rupture into the Subdural Space; Intracranial Tension and its Temporary Relief.

By W. G. SPENCER, M.S.

A BOY, aged 5 weeks, was sent into the Westminster Hospital by Dr. Francis, of Uxbridge, on account of rapidly increasing hydrocephalus, which had appeared since birth. The child was kept under observation for a month. It was otherwise a strong, well-nourished child and exhibited no other deformity. Both fontanelles and the sutures running into them were widely open. The measurements of the head were $18\frac{1}{4}$ in. in circumference at the level of the eyebrows, $10\frac{3}{4}$ in. from the occipital protuberance to the root of the nose, and the same between the tips of the mastoid processes. The pupils reacted to light; the disks looked grey; it was doubtful whether it could see. It could hear quite well. The cerebrospinal fluid obtained by lumbar puncture was found to be under normal tension; there was no leucocytosis; Wassermann's reaction was negative. Under observation the intracranial tension increased and vomiting became so frequent that it was difficult to feed the child. It frequently had screaming fits and held itself rigid, obviously on account of pain, but there were no special convulsions, rigidity, or paralysis. The temperature and pulse were about normal.

In view of the cases published by Dr. Keen and Mr. Ballance, in which the distended lateral ventricle was connected with the subdural space, I started with the object of giving relief by this method. Mr. Ballance kindly lent me a fine rectangular iridio-platinum cannula. When the very thin and soft bone was removed about 2 in. above the right ear the dura mater bulged, and on scratching it through, fluid spurted out to a height of 2 ft. The very thin dura matter was then widely opened and the fluid, in large amount, was found immediately beneath. Having enlarged the opening sufficiently to admit a strong light, I could see through the fluid the vessels of the pia mater, but the finger inserted through the opening entered the full length before the tip touched the cortex of the hemisphere. In order to establish an anastomosis between the subdural space and the loose connective tissue of the scalp the dura mater was cut away and the scalp undermined round the opening, and the wound sutured without drainage. For a day or two some fluid leaked out between the sutures, then the wound

healed by first intention, underneath which fluid distended the scalp. At first the symptoms resulting from the intracranial tension disappeared, and the child began to thrive; then the tension recurred. The fontanelles again bulged, and the fluid swelling under the scalp became less tense.

A month after the first operation the same procedure was carried out on the opposite side, and observations were made similar to those at the first operation. However, a month after the second operation intracranial tension again supervened rapidly; vomiting was so frequent that hardly any food could be retained. The pulse-rate increased to 160, and the child appeared about to die. Thereupon I re-opened both scalp wounds, and found the gaps in the skull, each of which was about 2 in. in diameter, blocked by oedematous, white, fibrous tissue. On removing this, fluid spurted out in quantities as before. In order to assure myself that there was no collection of fluid below the tentorium I exposed the lateral lobe of the cerebellum, to find that the folia were quite normal, and no fluid escaped. Then, in imitation of Mr. Sampson Handley's method, I took a double strand of plaited silk and passed it from the trephine hole under the scalp, down the back of the neck, over the dorsum of the scapula to the posterior border of the axilla. This was done on both sides. The wounds and punctures were all closed, and after some escape between the sutures, healed as before by first intention.

The intracranial tension recurred even more quickly and death seemed again imminent. I mentioned the case to Sir Victor Horsley, and he asked whether it would be possible to connect the subdural space with a venous sinus or vein, but the venous sinuses were so thin as scarcely to be visible, and the fluid was clearly so fibrogenous as to quickly plug any small communication. Then I called to mind the cases of cerebrospinal rhinorrhœa from injury of the base of the skull in the ethmoid region. So, ten weeks after the first operation, I made an incision in front of the coronal suture, just within the hairy margin of the scalp, turned downwards and forwards a flap and removed the frontal bone above the root of the nose. I thus exposed on each side the small frontal sinus, or rather, in this young child, the dilated upper end of the infundibulum. Next I cut away the thin dura mater, so that the fluid from the subdural space could freely flow down each infundibulum into the nose. After much fluid had escaped I saw clearly that the anterior end of the lateral ventricle bulged out as a finger-like projection, and I then assured myself that I had been dealing with a case of hydrocephalus

internus which had ruptured beneath the dura. The flap was sutured and healed by first intention. Fluid continued to flow freely down the nasopharynx. The skull fell in; the intracranial tension was better relieved than by the other procedures. For ten weeks there was nothing



FIG. 1.

Skiagram of head, antero-posterior aspect.

to note except that fluid escaped down the nose; the child's general condition simply became weaker. About a week before it died the flow of fluid seemed checked, but the passage of a blunt-end curved sound up each infundibulum without any re-opening of the frontal wound started

the flow again, and the child died seven months after admission, without any tension.

At the post-mortem there was an absence of all signs of suppuration, for except down the nose no external drainage had been employed. The head measured the same as on admission seven months before.

The skiagrams of the skull and the brain exhibit the usual appearance of hydrocephalus internus (figs. 1 and 2); the cortex forming

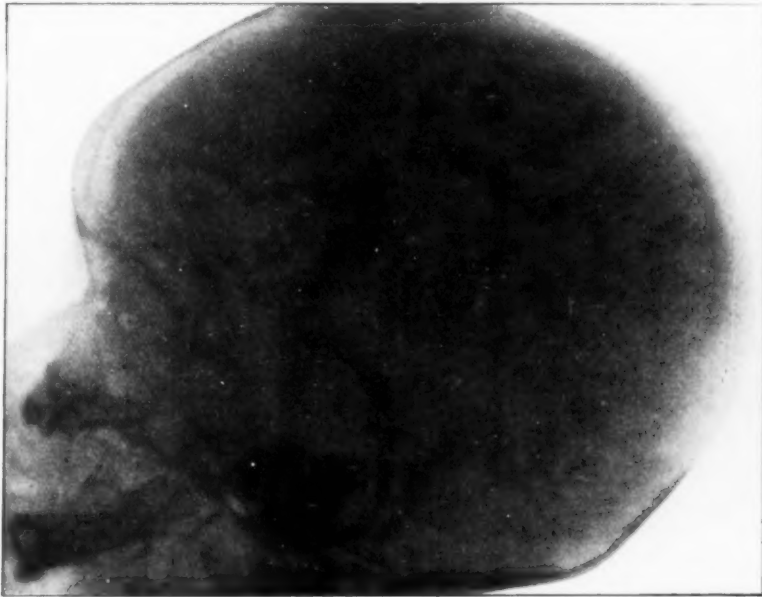


FIG. 2.

Skiagram of head, lateral aspect.

the wall of the distended lateral ventricle is extremely thin, in the region of the roof of the third ventricle it is reduced practically to the pia mater where it had ruptured. The gaps made in the skull were blocked by the œdematous, white, young fibrous tissue previously mentioned. The pons, medulla, cerebellum, ears, and rest of the body were normal. The silk strands inserted after Mr. Sampson Handley's method, when exposed by dissection, looked remarkably like nerves running in subcutaneous tissue. Each silk strand was closely

surrounded by a dense cylinder of white fibrous tissue with minute blood-vessels running longitudinally. Except for infiltration by young white fibrous tissue the silk was unaltered.

REMARKS.

The immediate object of the operative procedure was the relief of the pain and vomiting caused by the intracranial tension. After discovering the fluid beneath the dura I tried to find out something about hydrocephalus externus. My colleague, Dr. Hebb, recorded a case in which there was a normal brain surrounded by the fluid and a distended skull, the result of chronic tuberculous meningitis, and I was at first hoping that I had to deal with such a case.

*Hebb: Report of Post-mortem Examination made in 1896.*¹—Hydrocephalus externus: M., aged 1 year and 7 months. Body much emaciated; arms stiff and twisted inwards, so much that the palms nearly look forwards. Head large; frontal region bulging; anterior fontanelle large; sutures loose; ossification of calvarium irregular. Brain 24 oz. Dura much thicker than normal. On cutting through dura, quite half a pint of clear watery fluid escaped; this came from the intermeningeal space, and had exerted equal pressure on the brain, which was quite symmetrical, and except for its size was normal in appearance. The cerebral ventricles were quite normal, and the convolutions are well marked. There is no evidence of leptomeningitis. Greenish-yellow muco-purulent fluid in both middle ears. Tuberculous caseation in lungs and bronchial glands.

Other cases recorded under the heading of hydrocephalus externus also seem to have been what would now be termed tuberculous meningitis, acute or subacute.

I have not found the report of any cases in which a hydrocephalus internus had ruptured into the subdural space; there are, of course, many noted which have ruptured externally, especially during birth.

This case would clearly have been an unfavourable one for the drainage of the ventricle into the subdural space, and my attempts to drain the subdural space into the subcutaneous tissue of the scalp failed owing to the fibrogenous character of the fluid and its tendency to form young fibrous tissue. The objection to the drainage down the nose is that of liability to sepsis, which did not, however, occur in this case. As to any question of radical treatment for hydrocephalus internus, this case is quite unfavourable.

¹ *Westminster Hospital Reports*, 1897, x, p. 285.

This case has, I think, a physiological connexion, for the observations which I made on the child resembled those reported by Goltz¹ after the removal of the cortex of the cerebral hemispheres in dogs. Of three dogs, one lived fifty-one days, another ninety-two days, and the third dog, after living eighteen months, was killed. In this last dog the cortex of both hemispheres had been removed, also some part of the corpora striata and optic thalami. The paper gives a full account of the dog, and in conclusion a comparison was made between it and some lunatics in asylums.

In this child the cortex of the hemispheres would seem to have lost its function, except that of the temporo-sphenoidal lobes in relation to hearing. It never had convulsions, only rigidity when the tension became great. It moved all the muscles of the limbs, face, and larynx in a co-ordinate way; it showed desire and pleasure in connexion with food; it could hear the footsteps of the nurse drawing near and her voice; it certainly could not see at all, yet the reaction of the pupils remained normal.

Multiple Fibromata of the Tunica Vaginalis.

By G. H. MAKINS, C.B., F.R.C.S.

FIBROMATA developing in the subserous layer of the tunica vaginalis have been recorded by several observers, but the classical nature of the majority of the references shows that the condition must be regarded as a rare one. This opinion has been expressed by Mr. Jacobson² who quotes three cases of large single tumours. Professor Kocher³ quotes practically the same cases, and remarks that the tumours are usually highly lobulated, in some cases corresponding to the plexiform fibroma of Billroth. All the instances mentioned by these authors are of the single large variety. The classical case of Baizeau is a good example. In this the tumour was moulded upon the testicle, the lateral borders of the enveloping tumour gradually thinning away peripherally. The testis itself was normal. In two cases recorded by Mr. T. Holmes

¹ Goltz, "Der Hund ohne Grosshirn," *Arch. f. ges. Physiol.*, Bonn, 1892, li, p. 570, Taf. xii.

² "Diseases of the Male Organs of Generation," 1893, p. 434.

³ "Krankheiten der männlichen Geschlechtsorgane" (Billroth u. Luecke, "Deutsche Chirurgie," Lief. 50 b, 1887, p. 186).

and Mr. C. Heath, respectively,¹ a somewhat similar arrangement existed with regard to the testicle, and in both that organ was normal. In both the central part of the tumour was necrosing. A more recent observation of a case of this class has been published by Dr. Balloch²; in this instance a very large tumour of eight years' growth was met with in a negro, aged 16. The enlarged scrotum, pyriform in outline, with the apex directed downwards, extended nearly to the level of the knees. The skin was tense and the scrotal veins enlarged and prominent. Three separate masses were palpable, one at the external ring and two others below. The tumours, together with the testicle, were removed, also a quantity of redundant scrotal skin. The tunica vaginalis is described as "enlarged, thickened, and converted into a gelatinous mass." The upper tumour was attached in the inguinal canal by a pedicle, the other two were embedded in the tissues and shelled out readily. The tumours weighed together 38 oz., or with the tunica vaginalis 58 oz. The pathologist reported that "the main structure of the tumours was fibrous tissue, undergoing at many areas myxomatous and fatty degeneration. The tunica vaginalis was myxomatous throughout. The testis also showed areas of myxomatous degeneration. The tumours were classed as soft fibromata undergoing degeneration." Certain common characters appear to have been exhibited in all these recorded instances, thus slow growth, a tendency to reach a large size, softness in structure, and a tendency to degenerate or necrose when a certain size has been reached.

The case now recorded appears to differ from those above-mentioned (a) in the multiple nature of the tumours; (b) in the firmness of structure of the fibroma. It is shortly as follows:—

E. W., aged 27, single. As long as he could remember he was aware of the presence of some small nodules at the back of the right testis. The tumour first noticed might have been as large as a coffee-bean. Of late he had noticed that the tumours were both enlarging in size and increasing in number. On examination a group of nodules resembling a small bunch of grapes was felt at the back of the scrotum, some of which seemed united by a connecting cord. The nodules were elastic but very hard. The scrotum could be freely moved from the nodules, but they were firmly attached to the back of the testis and moved with the organ. The outline of the epididymis was somewhat

¹ *Trans. Path. Soc. Lond.*, 1869, xx. pp. 184, 286.

² *Ann. of Surg., Lond.*, 1904, xxxix, p. 396.

obscured, but the rest of the testis was normal in outline and consistence. The tumours were absolutely painless, and caused no inconvenience. The tumours were exposed by a vertical incision opening the cavity of the tunica vaginalis. It was then seen that the whole number were situated external to the cavity, two or three small tumours were on the surface of the cord, a large group was situated over the body of the epididymis, which was considerably thinned and narrowed, and two small tumours were on the outer surface of the testicle itself. No obvious connexion existed between the separate



Multiple fibromata of tunica vaginalis. ($\times \frac{4}{3}$).

tumours, and they were readily removed by dissecting the tunica vaginalis from the back of the testis and the surface of the spermatic cord. Except for the two small nodules attached to the outer surface of the body of the testis, which were removed separately, the accompanying illustration shows the entire chain connected by the strip of tunica vaginalis dissected away. The testis was replaced in the scrotum, the wound sutured, and the patient made a rapid recovery. Each of the small tumours is rounded in outline, on section pale and white, and microscopic examination shows them to consist of pure hard fibrous tissue.

I should have regarded this case as unique had I not met with the one quoted in Balloch's paper, reported by Tikhonovich.¹ The tumours were met with in a man, aged 26, and their development was attributed to a blow from the handle of an axe inflicted seven years previously. On palpation, tumours, varying in size from a lentil-seed to a large pea, were felt on the antero-interior surface of the left testicle, and at the upper end of the epididymis a tumour the size of a hazel-nut. The tumours were movable, both in relation to the testis and the scrotum. Operation demonstrated that the tumours were in the tunica vaginalis, covering the epididymis and the upper part of the testicle, the larger tumour being separate. As the vas deferens was involved with the smaller tumours the testicle was removed. On examination two nodules the size of lentil-seeds were found "in the testicle itself, in addition to those recognized before operation." Microscopic examination showed the nodules to consist of fibrillar connective tissue running in bundles, with spindle and round cells, the latter most marked along the course of the vessels.

Ontogenetically these tumours would seem to be identical with the small subserous fibromata occasionally met with on the intestine or beneath the parietal peritoneum. Their removal is indicated from their tendency to continuous growth, and in the case of the soft fibromata to degeneration and necrosis when a considerable size is reached. The testicle should be preserved if possible.

¹ *Khirurgia Mosk.*, x, p. 360.

Surgical Section.

May 14, 1912.

MR. CLINTON T. DENT, President of the Section, in the Chair.

The Surgical Treatment of Aneurysm.

An Address Introductory to a Discussion on the Subject.

By H. GILBERT BARLING, F.R.C.S.

I AM inclined to apologize for my temerity in introducing this discussion on aneurysm with the limited experience I have of the disease, but I feel to some extent absolved by the knowledge that, from the comparative rarity of the condition, many other surgeons would labour under similar disadvantage. It has seemed to me appropriate that the Surgical Section of the Royal Society of Medicine should take a formal opportunity of discussing the treatment of external aneurysms due to disease, because of the recent methods devised by Matas under the term of "endoaneurysmorrhaphy."

My own operative experience of external aneurysm, excluding traumatic cases, of which I do not propose to speak, is based upon five popliteal aneurysms, two aneurysms of the third part of the right subclavian artery with dilatation of the vessels on the proximal side, and one case of aneurysm of the internal carotid. Four of the popliteal aneurysms were treated by ligature of the superficial femoral artery at the apex of Scarpa's triangle. The only points concerning them worth mentioning are that two of them occurred in the same patient, a man aged 22, only a short interval supervening between the cure of the one and the appearance of the other, and that one patient, a male, aged 50, suffered from gangrene of the toes, for which a mid-tarsal amputation

was performed. The fifth popliteal case was treated by obliteration on Matas's method. Briefly the details are as follows:—

A male, aged 30, a long-distance runner, was admitted to the General Hospital, Birmingham, on June 28, 1910, with an aneurysm of the right popliteal space rather low down. The circulation was controlled by a rubber tourniquet and the sac laid open. The aneurysm was of the fusiform type, the popliteal artery opened into its upper end, and the anterior and posterior tibial arteries led out of the lower part; two other small arterial orifices were found opening into the sac. All the arterial openings were sutured with fine catgut, the sac was obliterated with the same material, and the wound was closed without drainage. Recovery was without incident of any kind, the foot remained warm throughout, healing was by first intention.

The patients with subclavian aneurysm were both males aged between 40 and 50; both complained of pain in the right shoulder, neck, and arm, and had been treated for rheumatism and neuritis. Treatment by rest, iodide of potassium, and modified diet made no impression on the disease, and as the pain was disabling, operative treatment was resorted to. The two cases were curiously parallel; in both the intention was to ligature the innominate artery, which was exposed by excision of the inner portion of the clavicle, but in both this vessel, the lower end of the carotid, and the first and second portions of the subclavian, were so dilated and atheromatous that the application of a ligature in either of these situations seemed likely to be followed by misfortune. As the limits of the aneurysms prevented ligature above the clavicle the first part of the axillary was tied and, simultaneously, the common carotid at the middle above the dilated portion. The aneurysms consolidated and there were no untoward symptoms of any kind. The first of the patients died five years after operation with an aneurysm of the arch of the aorta, which ruptured. The other patient lived five and a half years and died from cerebral mischief due to disturbance of the circulation, which in turn was the result of aortic disease, which had commenced at the time of the operation but developed rapidly a few months before death. Both of these patients were relieved of their symptoms, were restored to their duties, and enjoyed a fair measure of activity.

The aneurysm of the internal carotid occurred in a lady approaching middle age, who was quite clear that a small swelling had existed in her neck in the position of the aneurysm for many years, and that it had rapidly enlarged in the few months preceding my examination,

when it was the size of a bantam's egg and pulsed very actively both in the pharynx and in the neck. It was quite impossible to determine whether the aneurysm had developed from the upper end of the common carotid, from one of its main divisions, or from a branch of the external carotid. My incision first exposed the main trunk and then its divisions: when following up the latter a sacculated aneurysm was found springing from the upper end of the internal carotid just before it entered the base of the skull; the sac hung downwards like a pear on its stalk between the external and internal carotids, somewhat compressing the latter, and showing the possibility of an aneurysm bringing about its own cure; the lowest part of the sac just overlapped the bifurcation of the common trunk. The condition seemed favourable for Matas's restorative method, but I was deterred from this by the inaccessibility of the mouth of the sac close to the base of the skull and the difficulty of controlling the regurgitant stream of blood down the internal carotid if the suturing of the orifice proved faulty. Excision of the aneurysm was therefore resorted to. A few days after the operation the patient complained of pain and weakness in the left shoulder, which was followed by some wasting of the muscles, but these have now recovered. We have, however, in this incident another reminder of the possible risks of ligaturing one of the main arteries supplying the brain, and the desirability of adopting the restorative method when this is applicable.

Aneurysm of the internal carotid appears to affect women more commonly than men. It is apt to extend towards the pharynx and to burst into that cavity, whilst more than once it has been opened there by the surgeon's knife when obscured probably by an inflammatory condition around the sac.

A few words may not be out of place as to the material for ligature in continuity and the method of its application. Personally I prefer an absorbable ligature, and I think none is better than moderately chromicized catgut, which I have used for arteries of all calibre up to the common iliac, without drawback of any kind. I do not think either kangaroo or reindeer tendon quite so manageable as catgut, and the knot produced is undesirably bulky, a factor which has been accused by more than one surgeon as a source of misfortune by ulcerating into the vessel. Floss silk has much to recommend it; it is easily sterilized, it is strong and very manageable, but it has one serious drawback: although it may be absolutely sterile when applied to the artery, if any wound infection occurs the interstices of the silk become invaded by

organisms, and it will probably ulcerate its way through the walls of the vessel. This is shown in two successful cases of ligature of the innominate, one by C. J. Symonds and one by W. B. Burns, of Memphis. The silk ligature used was recognized in the discharge from the wound, and it is easy to imagine the peril to the patients' lives which this implied. If an absorbable ligature should become infected, it would probably not cut its way through the carotid wall, as would silk.

As to the method of ligature, I prefer the stay-knot of Ballance and Edmunds to any other. My intention has always been to close the artery with as little damage as possible; division of the internal coat has appeared to me to be a gratuitous injury. But if a great artery is to be closed without this damage a double ligature is necessary, the first to break the force of the blood-current, whilst the second is applied under more favourable physical conditions side by side with it. The stay-knot, with which everyone is now familiar, provides exactly what is required and disturbs the vascular supply to the arterial walls as little as a single ligature.

It is impossible to leave this part of the subject without referring to the influence of Lister's work on the treatment of aneurysm. In no department of surgery is asepsis of more vital importance; it transcends in value even the gift he bestowed on us of the absorbable ligature. Only when the quite recent history of operative work on aneurysms comes to be written and compared with that of preceding years shall we realize what a profound and vitalizing influence our great master exercised on a subject which was at the same time a fascination and a terror to the surgeons who preceded us. To Lister I owe it that my own small experience has been practically without anxiety; there has been no wound infection, and as a consequence no secondary hæmorrhage.

The procedures devised by Matas under the title of endoaneurysmorrhaphy offer a bold challenge to the methods we have hitherto relied on. The essence of his work is that the diseased vessel is attacked from within instead of from without and that the sac is obliterated, no aneurysmal cavity being left in which recurrent pulsation or inflammatory troubles may arise. He relies on the activity of the endothelium lining the sac of the aneurysm, and especially upon that lining the orifices of vessels opening into the sac, when approximated by suture to unite and close the vascular orifices and to obliterate the sac. The advantages claimed for endoaneurysmorrhaphy as against proximal ligature are that the former avoids three of the difficulties of the latter:

(1) damage to the vessel wall through the vasa vasorum, which exposes the patient to the possibility of secondary hæmorrhage at the point of ligature; (2) failure to cure the aneurysm from too free an anastomotic current through the sac; and (3) pressure on the collateral circulation by the distended sac, predisposing to gangrene.

The advantages of endoaneurysmorrhaphy over excision of aneurysm are claimed to be that the main vein is less likely to be injured, that the collateral circulation is less disturbed, since the only vessels interfered with are those opening into the sac itself, and as a consequence gangrene of the distal parts is less likely to occur. A further advantage claimed for Matas's method over proximal ligature or excision is the possibility in selected cases of restoring the vessel wall by suture in such a manner as to leave the main blood channel of the distal parts still patent whilst the sac of the aneurysm is obliterated. Although it seems almost unnecessary, yet for the sake of clearness it is advisable briefly to describe and illustrate what Matas proposes. He recommends three different procedures adapted to aneurysm of varying kinds.

(1) *The Obliterative.*—In this the orifices of the main vessels entering and leaving the sac and of any smaller arteries which may be found in it are closed by suture and the sac itself is obliterated, also by sutures. This is the method usually adopted in fusiform aneurysms.

(2) *The Reconstructive.*—In certain cases of fusiform aneurysm where the proximal and distal orifices of the main vessel are not very far apart and where there is a distinct groove indicating the position of the original arterial channel, the wall of the sac is sutured over this groove so as to remodel the arterial wall that it may again carry the blood-current. The orifices of smaller arteries in the sac are then sutured and the sac is finally obliterated.

(3) *The Restorative.*—This is applicable to sacculated aneurysms in which the sac communicates with the artery by an orifice well defined and of moderate extent. The simple orifice is sutured so as to repair the arterial wall and only rarely do secondary orifices require attention. The sac is then obliterated by suture as in the other procedures.

Whichever plan is adopted, an essential point is the complete control of the arterial circulation; it is necessary to dominate not only the proximal but also the distal vessel or vessels. This is easy to attain in the limbs when Esmarch's ligature can be applied to the part above the aneurysm, but is far more difficult in the abdomen, in the neck, and where the limbs join the trunk. In such positions the control of the circulation seems to be best attained by clamps applied to the main

artery above and below the sac and as close to it as possible. Even then a large collateral opening into the sac, as, for example, the deep epigastric into an iliofemoral aneurysm, may give rise to troublesome and even severe hæmorrhage, and clamping of this vessel would also be required. Aneurysm in the abdominal cavity is treated exactly as in the limb, the sac being obliterated without drainage, and the peritoneum closed over it as the skin would be in the other parts. As to the suture material, catgut, silk and thread have all been used with success. When the sutures are inserted they should not be used mincingly, but should take a good hold of the walls of the sac, without, however, perforating its whole thickness. To obtain obliteration tension mattress sutures are generally necessary; they should take a good hold of the walls of the more superficial parts of the sac, then pass through the overlying skin, when they are tied over rolls of gauze.

Endoaneurysmorrhaphy has attracted more attention on the American continent than in Europe, and to the results attained there we must first direct our attention. Dr. Matas published his last collection of cases in 1910,¹ but I learn from a personal communication that he will shortly place the results up to the present time before the American Medical Association. The record just referred to comprises 149 operations for aneurysm, of which 105 were oblitative, 20 restorative, and 24 reconstructive. Of these, 129 occurred in the external iliac or in its continuation down to the popliteal. In only 5 cases did gangrene follow operation; these were all obliterations, and in three of them the principal factor which determined gangrene was injury and ligation of the popliteal vein.

The mortality is not given in the paper alluded to above, and it is therefore necessary to refer to an earlier collection of cases by Matas,² which comprises 85 operations—59 oblitative, 13 restorative, and 13 reconstructive. The figures are not quite clear, as in one place 8, and in another 7, deaths are referred to, but I am only able to identify 7. Six of these occurred in the oblitative group, 2 were aneurysms of the abdominal aorta, 1 of the external iliac, 1 was iliofemoral, 1 femoral, and 1 popliteal. The remaining death was after reconstruction in the iliofemoral region; the restorative operations were free from mortality. Secondary hæmorrhage happened in 2 cases only; both were obliterations. Relapse followed operation four times, always after reconstruction; 1 of these patients was cured by an

¹ *Trans. Amer. Surg. Assoc.*, Philad., 1910, xxviii, pp. 4-54.

² *Journ. Amer. Med. Assoc.*, Chicago, 1908, ii, pp. 1667-71.

obliteration, 2 were submitted to amputation and recovered, the fourth died after rupture of the sac.

In the later paper it is definitely stated that gangrene had not occurred in any of the restorative or reconstructive operations then collected, nor had relapse in any other instances than those referred to above.

The figures which I am able to bring forward regarding endo-aneurysmorrhaphy in the British Isles are very meagre, though I have made careful search and inquiry. The total number of cases is 16, 9 collected from current literature and 7 yet unpublished from notes kindly provided by my surgical friends. Of these 16 aneurysms, 1 was of the external iliac, 1 femoral, 11 popliteal, 2 subclavian, and 1 brachial. Fourteen were operated upon by the obliterative method; of these, one patient with external iliac aneurysm died from sepsis. Gangrene of the leg supervened in this case and in one with popliteal aneurysm. The two remaining operations were reconstructive in patients with popliteal aneurysm; in both the sac had already ruptured and both operations were followed by gangrene. Secondary hæmorrhage or failure to cure is not referred to in any of the cases. We have, therefore, one death only, and apart from this case gangrene following operation in three other patients, all of whom recovered after amputation. (See Table.)

Comparison between these results and those obtained by other methods is not easy, but my table of 11 popliteal aneurysms reveals the misfortune of gangrene occurring in 3 patients, all of whom recovered after amputation, and with these we may contrast the results collected by Rigby from the London Hospital records.¹ The series includes 19 cases operated on for popliteal aneurysm by various methods other than that of Matas. Four of the patients suffered from gangrene of varying extent, 1 from secondary hæmorrhage, and 2 died as the result of the operative proceedings, but in both of them the sac had ruptured.

Argument in favour of particular methods based on statistics is difficult to apply in connexion with aneurysm, partly on account of the rarity of the disease, and partly on account of the varying conditions requiring treatment. I do not propose, therefore, to express any dogmatic opinion on the value of the new treatment as compared with the older methods. Probably that surgeon will obtain the greatest

¹ *Proc. Roy. Soc. Med.*, 1909-10, iii (Clin. Sect.), p. 131.

TABLE GIVING DETAILS OF SIXTEEN CASES OF ANEURYSM TREATED BY END ANEURYSMORRHAPHY IN THE BRITISH ISLES.

No.	Position of aneurysm	Nature of operation	Typical or atypical	Result	Remarks	Reference
1	Subclavian, second and third parts Brachial	Ligature of first part of subclavian and infolding of sac without opening	Atypical	Recovery	—	Moynihan, Leeds, unpublished
2		Obliteration				
3	External iliac	"	Typical	"	Septic peritonitis; gangrene of leg; furious bleeding from deep epigastric and circumflex iliac arteries when sac was opened	Walter Thompson, Leeds, unpublished Sinclair White, Sheffield, unpublished
4	Popliteal	"	"	Recovery	—	Graham Simpson, Sheffield, unpublished
5	"	"	"	"	Popliteal vein damaged and ligatured; gangrene of leg; amputation	Thelwall Thomas, Liverpool, unpublished
6	"	"	"	"	—	Barling, Birmingham, unpublished
7	"	"	Atypical	"	Sac too fragile to carry sutures; operation concluded by tying entering artery	Anonymous, unpublished
8	"	"	Typical	"	—	Rigby, <i>Proc. Roy. Soc. Med.</i> , 1909-10, iii (Clin. Sect.), p. 131
9	"	"	"	"	(Same patient as No. 8)	<i>Idem, ibid.</i>
10	"	"	"	"	—	Rigby, <i>Clin. Journ.</i> , 1909, xxxiv, pp. 261-64
11	"	"	"	"	—	Barker, <i>Lancet</i> , 1911, ii, p. 871
12	"	"	"	"	—	Maynard Smith, <i>Proc. Roy. Soc. Med.</i> , 1909-10, iii (Clin. Sect.), p. 130
13	"	Reconstruction	"	"	Reconstructed artery seen to pulsate; gangrene of foot; amputation of thigh; the sac had ruptured	Shoen, <i>Clin. Journ.</i> , 1910-11, xxxvii, pp. 77-80
14	"	"	"	"	The sac had ruptured; reconstructed artery seen to pulsate; gangrene of toes	<i>Idem, ibid.</i>
15	Femoral	Obliteration	"	"	The sac had ruptured; it could not be entirely obliterated; drained	<i>Idem, ibid.</i>
16	Subclavian, third part	"	"	"	Aneurysm exposed by division of clavicle; traction ligature distal to aneurysm failed to control reflux current of blood, so vessel was clamped on distal as on proximal side of sac	Pringle, <i>Edin. Med. Journ.</i> , 1911, n.s., vii, pp. 253-7

success who restricts himself to no single line of treatment, but selects that most appropriate in the case immediately before him. For example, influenced by my two successful cases of subclavian aneurysm, I should in similar circumstances again tie the axillary and the common carotid, but I am very favourably impressed by the advantages of endoaneurysmorrhaphy and shall gladly adopt it under suitable conditions. Obliteration is likely to hold the field for the majority of cases; it may be fairly said to have proved its claims. In carefully selected cases restoration of the artery promises brilliant results, and should, I think, certainly be adopted where possible. Reconstruction has not so clearly established its claims, and should, I think, be used but rarely and when the conditions for reconstruction are unusually favourable.

In conclusion, I would like to express my admiration for the scientific and skilful work of Dr. Matas in injuries and diseases of the vascular system.

DISCUSSION.

Mr. C. B. LOCKWOOD said that his own experience of ligature of vessels for the cure of sacculated aneurysm was confined to only five cases, and in each of those the aneurysm was a popliteal.¹ Though so few, they were to him very interesting, and from them he had learned much, so he might be pardoned for mentioning some of the circumstances attending them. He was greatly struck by the way in which these sacculated aneurysms of the popliteal artery and elsewhere leaked, and the disastrous effects of that leaking. A policeman was lying in bed with an aneurysm of the popliteal artery, and in the middle of the night he was seized with a violent pain. Nothing seemed to have occurred at the seat of the aneurysm, but on the following day, when the artery was tied, some blood was found extravasated along the course of the vessel. It was possible that, during a struggle which the policeman had had he ruptured his popliteal artery, and the final leakage took place during the night. Again, whilst tying the superficial femoral artery of an old man it was obvious that leakage had taken place

¹ I find that the left subclavian artery was successfully ligatured for axillary aneurysm on April 10, 1906. [C.B.L.]

without apparent cause, because at the seat of the ligature some old extravasated blood was met with. Though the arteries of that patient were calcareous, he pursued an uneventful course towards recovery. In a third case the effect of the leakage was more disastrous. A patient with popliteal aneurysm had some blood extravasated in his popliteal space, and that had brought about the usual results, for the tissues were inflamed and œdematous. He could not help thinking how easy it would have been for anybody to have mistaken that swelling for an abscess. The popliteal artery was tied; and there he believed he fell into an error. Twice before he had tied a superficial femoral artery, although some leaking had taken place. But this time the result of the operation—leaking having occurred—was that there was some gangrene of the skin of the foot and the leg.

The next step in that case was to open the aneurysm and turn out its contents. After a rather long period of confinement to bed the patient recovered sufficiently to be able to leave the hospital and go to a convalescent home. He came back, and then his aneurysm had gone, the leg was in fairly good condition, and the ulceration had healed. But as soon as he returned to work the skin again became ulcerated, and in the end he had to have amputation done through the lower third of the thigh. Another patient was interesting in a different way: He had a very thin-walled sac, with very marked pulsation in it. In addition he had $1\frac{1}{2}$ per cent. of sugar in his urine, which led to the conclusion that the arterial degeneration might be extreme, and also caused anxiety as to the ultimate result of the ligaturing. The superficial femoral artery was ligatured, and the aneurysm, after being quiet for a time, began again to pulsate, but afterwards consolidated and got well. During the convalescence from this operation he suffered from extreme neuritis, which took a considerable time to get well. The last case to which he would allude was that of a patient with popliteal aneurysm which had become consolidated but remained as a large, painful lump in the popliteal space, incapacitating the patient from his occupation. That he attempted to dissect out. After prolonged and difficult dissection he found that the aneurysm was so much incorporated with the walls of the popliteal vein that the latter was almost certain to be opened; indeed, there was considerable bleeding from it and which was stopped by a fine continuous suture. So the aneurysm was laid open and packed, and in that case also there was recovery. Therefore his experience had been very small indeed, but, to him, not uninteresting. He had been much impressed with the urgency of these cases of sacculated

aneurysm ; it was not a matter for delay, but for very speedy operation. With regard to the details of the operation, he had always used fine silk, No. 3 or No. 4 twisted silk. He had taken care to clear the artery with a sharp knife, not employing a blunt instrument, and to sew the sheath of the artery over the ligature.

He would like to mention two interesting aneurysms which he had seen. He noticed a mesenteric aneurysm in the present collection. Once, at the Great Northern Hospital, he had seen an aneurysm of the superior mesenteric artery. The diagnosis was obvious, and he was anxious to be allowed to ligature the artery. But that could not be done, and the aneurysm afterwards burst and extravasated into the abdomen, and the patient died. He thought that specimen must be in the Great Northern Hospital Museum, but he did not know whether that rare and unusual case had been recorded. He saw also in this collection an aneurysm of the dorsal artery of the foot. He remembered, a few years ago, seeing an aneurysm of that artery which was cured by operation. With regard to what had been said about Matas's method of restoration, one could not help feeling a certain reluctance to perform a plastic operation upon a diseased structure, and he felt inclined to question whether it was correct to suppose that in these aneurysms the seat of the suture possessed that endothelial lining which was said to have such reparative properties.

Mr. D'ARCY POWER, speaking for himself and Mr. G. H. COLT, said: The subject of aneurysm is of perennial interest, and the Section of Surgery in the Royal Society of Medicine has done well to review the progress made in it during the last few years. We do not see many cases of aneurysm in the surgical wards of our general hospitals. They are either treated in the various smaller hospitals, they remain untreated by surgical methods, or they are less numerous now than they used to be when more alcohol was drunk, and syphilis was less systematically treated. But in spite of the scarcity of cases much has been done of late years in the treatment of aneurysm, and the work of Matas and other distinguished surgeons has shown how much the advance of surgery has enabled aneurysms to be cured by the most radical methods. It is clear, however, that it is impossible to treat every case of aneurysm surgically by these obliterative methods without undue risk to the patient. There will always remain some abdominal and, more rarely, thoracic aneurysms which from the accident of their position or anatomical relationships cannot

be excised or sutured. For these aneurysms some method of introducing wire into the sac, with or without electrolysis, remains as the simplest and least dangerous method of treatment.

Until the year 1903 the method of wiring was unscientific, and was carried out with comparative disregard of aseptic principles. The aneurysm was exposed, a trocar and cannula were thrust into its wall, the trocar was withdrawn, and as much wire as seemed enough was passed into the sac by pushing it through the cannula. This method involved a good deal of handling both of the sac and the wire, the wire often kinked and became unmanageable, the hæmorrhage was severe though controllable, and the introduction of the wire occupied a considerable time.

(a) The results of wiring without electrolysis and performed by the older method are as follows:—

Between 1864 and 1900, 14 cases were treated, of which 8 were thoracic and 6 abdominal. In the 8 thoracic cases all the patients were in a desperate condition and died from various causes from four days to one month after operation. In the 6 abdominal cases, one patient (Langton's) lived eleven years and ten months, and died at Acton on February 9, 1910, probably from rupture of the sac. No post-mortem examination was made. The patient was a woman, aged 37 at the time of the operation, and the aneurysm was noticed shortly after delivery. Five feet of silver wire had been used. There was some doubt as to whether or not the patient was syphilitic, but when she was again admitted into St. Bartholomew's Hospital under Mr. Bruce Clarke in 1907, it was noticed that she had irregular and dead white scars on the forehead and behind the left knee, and she then gave a history of miscarriages. This is the only case on record in which the presence of coils of wire was demonstrated in the sac during life by an X-ray examination. They appeared as oval loops. One patient (Morse's) lived four years, and died after receiving a kick on the abdomen. Five and a half feet of silvered copper wire had been used. One patient (Loreta's) died thirteen weeks after operation of rupture of the aorta at the origin of the sac, which was completely filled with laminated clot and wire. Six and a half feet of silvered copper wire had been used. Two patients were in a desperate condition, and death occurred soon after the operation. In one case (Stevenson's) death was probably hastened. Since 1900 one patient had his abdominal aneurysm wired by Mr. Harrison Cripps, and lived eighteen months, after which time he could not be traced. (This

case is unreported.) One patient, in whom Colt's instrument No. 1 was used, died fifty hours after operation.

(b) The results of wiring by the older method combined with electrolysis between 1864 and 1910 are as follows:—

Of 29 thoracic cases, 2 patients in whom the aneurysm involved the origin of the left subclavian died, one on the second day and one on the twentieth day. Two in whom the aneurysm involved the origin of the innominate artery died—one two months and one fourteen months after the operation. Of the rest, 1 died three and a half years after the operation, 1 was alive three years later at the time of the last report in October, 1910, and 20 others died at periods varying from two and a half days to ten months, the average duration of life being fourteen and a half weeks. One was alive three months after operation at the time the report was made. Many of these patients were in a desperate condition, and the relief of symptoms was well marked. Of 7 abdominal cases, 1 died five years after operation, 1 died eight months afterwards from dysentery, 1 died forty-seven days afterwards, 1 died twenty days later, and 3 died from five and a half to forty hours after operation.

In 1903 one of us (G. H. Colt) invented an instrument for the rapid introduction of a known quantity of sterilized wire into an aneurysm, with a minimum of disturbance. The method was described and the instrument was figured in the *Transactions of the Royal Medical and Chirurgical Society*¹ with an account of the case in which it was used. The ease with which the wire was introduced defeated the object of the operation, for, as is seen in the specimen (Museum of St. Bartholomew's Hospital, No. 1551D), a loop of wire left the sac and entered the aorta. Up to the present time six cases are recorded in which this accident has happened independently of the size of the opening of the sac, by the older method of wiring through a cannula. (1) In Ransohoff's case of aneurysm of the ascending arch, the opening of the sac was 1 in. in diameter and a loop of wire had passed towards the heart. (2) In Reeves's case of abdominal aneurysm the opening of the sac was 1 in. in diameter, and a loop of wire had passed 10 in. up the aorta, one loose end passing as far as the aortic valves. (3) In the case of aneurysm of the ascending arch recorded by White and Gould, the opening of the sac admitted four fingers, and a loop of wire had

¹ *Med. Chir. Trans.*, 1903, lxxxvi, pp. 362-76.

passed into the aorta. (4) In Griffith's case of abdominal aneurysm the mouth of the sac was $1\frac{1}{2}$ in. long, and narrow, and a double loop of wire had passed $2\frac{1}{2}$ in. up the aorta. (5) In Ballance's case of aneurysm of the ascending arch, the wire had been previously coiled into a cylinder $2\frac{1}{2}$ in. in diameter, but the free end passed up to the middle of the left ventricle and loops of wire had also passed down the aorta for $2\frac{1}{2}$ in. (6) In Power and Colt's case of abdominal aneurysm mentioned above, the opening of the sac measured $2\frac{1}{8}$ in. and a loop of wire 7 in. long had travelled up the aorta. In this case Colt's instrument No. 1 was used; it delivered coils of snagged wire $1\frac{1}{2}$ in. in diameter.

In view of this occurrence another instrument (No. 2) was arranged to sever the coils from time to time without removing the needle from the sac, but this instrument was never used, because the principle and design of instrument No. 3 proved to be so much better. This instrument was described and figured in the *Lancet*¹ and in the *Transactions of the Fifteenth International Congress of Medicine*, held at Lisbon in 1907. The instrument consists of a trocar and cannula with which the sac is pierced; an additional barrel can be attached to the cannula, and this barrel contains a light wire frame in the form of a cage, or a wisp which is pushed through the cannula by means of a piston until it reaches the sac, where it opens out like an umbrella. The cages and wisps are made in different sizes, of fine, lissom steel wire, dull gilt, and the surface area presented for clotting may be calculated with great accuracy. The following is a summary up to the present date (May, 1912) of the cases of abdominal aneurysm treated by means of Colt's apparatus (No. 3) without electrolysis:—

(1) A male patient who died four days after operation from a rupture of the sac into the peritoneal cavity. The rupture was not at the seat of puncture, as was shown post mortem. The case was under the care of Mr. D'Arcy Power and is mentioned in full later.

(2) A male patient died two days after operation from ether pneumonia. In this case the wires were found at the post-mortem examination to be evenly expanded inside the sac, and there was a firm and uniformly adherent clot—a point which is in favour of the dull gilt wire employed. The specimen was taken to St. Bartholomew's Hospital Museum, but was lost. It is recorded by Lieut.-Colonel M. P. Holt, D.S.O., R.A.M.C., in the *Journal of the Royal Army Medical Corps*.²

¹ *Lancet*, September 19, 1903, pp. 808-13.

² *Journ. Roy. Army Med. Corps*, 1904, iii, pp. 175-78.

(3) A male patient operated on in Dublin, who died two months after, apparently from leakage of the sac. The case is unpublished.

(4) One male patient, living at the time of the report.¹ Mr. de Courcy Wheeler writes: "The present condition may be summed up by saying that aneurysm may still be diagnosed, but it is better and not worse than it was two years ago. The patient was aged 38, with a good family history. He had served in the Army for sixteen years, during which time he contracted syphilis. For the last seven years he was employed in Guinness's brewery. His symptoms began eight months before he was admitted to the hospital, in August, 1910. Dyspepsia and pains in the back were the worst symptoms until July, when he noticed the abdominal pulsation. He was kept under rigid medical treatment for five weeks, but even in this short time the symptoms became more severe and the pulsation in the abdomen obviously increased. There was a loud systolic murmur below the tumour in the region of the bifurcation of the aorta, traceable downwards along the iliac vessels. There was no murmur over the tumour. Expansile pulsation was easily demonstrated. The diagnosis of aneurysm of the celiac axis was made. On August 30, 1910, the aneurysm was easily isolated and appeared like a distended and thin-walled gall-bladder, somewhat larger and more oblong than an orange. The sac gave an uncomfortable feeling of thinness and friability on manipulation. The origin of the tumour was lost in the aorta in the region of the celiac axis, and it was quite impossible to determine the exact vessel from which it sprang. Probably the aorta and all its branches in this region were involved. A trocar and cannula were plunged for about 2 in. into the sac, the point of the trocar aiming, as far as could be estimated, at the mouth of the vessel leading into the sac. When the trocar was removed the blood welled out without any expulsive force. A cartridge containing a cage of 150 in. of Colt's wire was applied to the mouth of the cannula, through which the wire was pushed into the aneurysm by means of the piston. There was no further bleeding, but the puncture point in the sac was strengthened by a few sutures passed through the wall of the sac. The operation was performed in a very short time. For the first five days the pulsations of the aneurysm were more tumultuous, and it was deemed advisable to give hypodermic injections of morphia to ensure absolute quietude on the part of the patient, who was restless and uneasy. After the fifth day the pulsations became less, the pain in the back

¹ Wheeler, *Brit. Med. Journ.*, 1911, ii, p. 1001; Case I.

disappeared, and the tumour—allowing for the resistance of the lines of buried suture in the abdominal wall—was harder and slightly reduced in size. Six weeks later the man was discharged from hospital after an intramuscular injection of '606.' A second intravenous injection was given recently owing to the presence of a positive Wassermann reaction. After another short interval he resumed light work at the brewery." Mr. Wheeler adds there is little doubt that the progress of the aneurysm towards disaster was checked by the operation. Time alone will show the exact part played by the wire in bringing about so satisfactory a result.

(5) A male patient was living at the time of the report,¹ one month after operation, and showed disappearance of the bruit and reduction in the size of the tumour. The man was aged 30, and presented symptoms so like the previous case that it was unnecessary to enumerate them. Pain in the back was again the prominent symptom, and it drove him to seek relief. He was given an intravenous injection of "606" and, a week later, an intramuscular injection of horse serum immediately before the operation. At the operation the pancreas was found to be firmly adherent to the front of the sac above. The liver did not appear and the stomach presented an anterior relationship below. The aneurysm was as large as a big orange. It appeared to spring from the aorta below the origin of the cœliac axis. The splenic vein, together with the gastro-hepatic omentum, impeded access to the front of the sac. There was no bleeding whatever in this case when the cannula was withdrawn after the wire had been introduced, nor on removal of the trocar before the cartridge was put into position. A wisp of 105 in. of wire with a surface area of $2\frac{1}{2}$ in. was used in this case instead of a cage. In suturing the puncture the needle injured the splenic vein, but the oozing was easily controlled. In this case the pulsations were more tumultuous and intense for a few days after the operation, whilst the pain in the back was very severe. After the fifth day, however, all pain and discomfort had gone and there was no trace of the loud murmur which had been present before the operation. There was no doubt that the tumour was considerably reduced in size four weeks later, and the consistence had become hard and firm. Mr. Wheeler writes (May 8, 1912): "This patient was operated upon in July, 1911. I saw him two months ago, and there was no sign of the aneurysm beyond an increased resistance under the scar of the operation. He was perfectly

¹ Wheeler, *Brit. Med. Journ.*, 1911, ii, p. 1091.

cured, and he has passed, as sound, a medical examination in London for a Government post in the Naval Reserve."

(6) A male operated upon by Mr. Wheeler (hitherto unpublished). He died of intestinal obstruction owing to the performance of gastro-enterostomy for dilated stomach after the wire was introduced into the aneurysm. Mr. Wheeler says: "The loop of jejunum which I fixed to the posterior wall of the stomach got pressed upon by the aneurysm behind and the stomach and abdominal wall in front, a most unlooked-for complication. At a second operation, two days later, the obstruction was quickly relieved, but subsequent vomiting ruptured the aneurysm at a point remote from the position of puncture for the wire. The examination showed that the wire had entered the aneurysm between two layers of clot already formed—a point, I think, of practical importance, because it tells us that we must get a good flow of blood through the cannula before introducing the wire, so as to be sure that the instrument is in the lumen of the aneurysm and not burrowing between laminated clots."

(7) A male patient¹; lived for several weeks and eventually died of pneumonia after leaving the hospital. There was no post-mortem examination. The case was under the care of Professor Conway Dwyer, who writes (May 10, 1912): "The pain which, before the operation, was severe and continuous, disappeared completely, and the pulsation had almost gone. I heard that some months afterwards he was admitted to another hospital suffering from pneumonia. He died there, but I have not been able to get particulars."

(8) Major C. B. Lawson, R.A.M.C., also sends us details of the following case: A man, aged about 33, whose previous occupation had been a boiler tube maker, was a private in the Lancashire Fusiliers. There was no history of syphilis, but there was a history of severe injury to the abdomen, as he was thrown from his horse on to an anthill during the South African War. He had an aneurysm as large as a tangerine orange between the celiac axis and the superior mesenteric artery. It communicated with the left side of the aorta and extended in the direction of the left kidney. An epigastric laparotomy was performed on May 6, 1906; the tumour was exposed by incising the lesser omentum and drawing down the stomach and pancreas. The fundus of the sac was very thin. Wisp No. 2 was inserted, and three days afterwards the tumour was more distinct and very hard, but there was no expansile pulsation. Pulsation in the anterior and posterior

¹ Wheeler, *Brit. Med. Journ.*, 1911, ii, p. 1091.

tibial arteries was more marked than before the operation. The pulse-rate after the operation was greatly increased for about a week. The case was invalided to Woolwich, and the patient was alive and well four years and nine months after the operation, but we have no report after February, 1911.

(9) A male patient, probably suffering from an aneurysm of the ascending part of the arch of the aorta. The right carotid and sub-clavian arteries had been tied two years previously. The patient was in a desperate condition from thinning of the front of the sac. He died of external hæmorrhage seven days after the operation, but the bleeding did not occur at the site of the scar. (Unpublished.)

The first case mentioned in our summary was that of a male, E. S., aged 36, admitted into St. Bartholomew's Hospital on March 5, 1911. He began to have attacks of severe pain in the right hypochondrium in October, 1906. The pain doubled him up and made him lie down. The attacks came on without warning and could not be assigned to any cause. At first they lasted about ten minutes at intervals of a week, but they have gradually become more frequent, longer, and more generalized, though they are worst in the small of his back. He has been confined to his bed for the last month. Seven years ago he received a severe blow in the epigastric region from the handle of a winch. Examination showed that he had a pulsating globular swelling in the middle line of the abdomen, 2 in. below the xiphisternum. There was a bruit over the swelling. Enlarged and discrete glands were felt in the left axilla, and there was a small gland in the right axilla and in the right supraclavicular region. The patient was shown "at consultations," and the general opinion was expressed that he was suffering from malignant disease of the pylorus and that the enlargement of the glands was due to secondary deposits. The tumour was explored on March 18, and was found to be an aneurysm of the celiac axis. A wire wisp was introduced by Colt's apparatus, but no blood escaped from the cannula when the trocar was withdrawn, so that it is probable that the wisp never entered the sac at all. The edges of the perforation were closed with two silk sutures and the abdominal wall was closed in layers. The operation took twenty-four minutes, including the anæsthetic and dressing. The patient went on well after the operation until 7 p.m. on March 22, when he died suddenly and without any warning. The post-mortem examination showed that he had a pathological aneurysm of the celiac axis which had ruptured into the lesser and greater sacs of the peritoneal cavity. The wire lay between the layers of a previously formed clot. There was no leakage.

The summary of these cases in tabular form reads as follows:—

Abdominal.—One patient alive and well four years and nine months after operation (last report, February, 1911); 1 patient alive and well one year and eight months after operation (last report, May, 1912); 1 patient alive and well nine months after operation (last report, May, 1912); 1 patient lived some months and died of pneumonia; 1 patient died two months later of leakage from sac; 1 patient died four days afterwards from rupture of sac, not at site of puncture; 1 patient died a few days after operation from acute dilatation of stomach; 1 patient died two days after operation of ether pneumonia. The 3 patients who are alive and well have been entirely relieved of their pain. Death was probably hastened by a few days in two of the cases which ended fatally.

Thoracic.—One patient died of rupture of the sac externally, but the rupture was not at the seat of puncture.

At the discussion held at the Royal Academy of Medicine in Ireland on December 16, 1910,¹ one of the speakers referred to the risk of embolism after the operation, and until the present time it has always been held to be a distinct risk. Taking all the cases recorded up to 1910 in which wire has been introduced into an aneurysm, there are 33 in which the lesion was situated on the cardiac side of the origin of the left common carotid artery, and in 22 of these the aneurysm lay between the heart and the origin of the innominate artery. In only one case were there any symptoms of cerebral embolism, and even in this case it was doubtful, yet altogether there were fifty-five large direct arterial channels open to receive a fragment of clot from the aneurysm and to carry it to the brain. No case of embolism of the vessels of the upper extremities has been recorded in aseptic cases. In no case has embolism of the arteries of the lower extremities been recorded when abdominal aneurysms have been wired. In cases treated by Macewen's method the evidence is entirely against emboli being detached by scratching the wall of the sac. We know of one patient in whom needling was performed on twenty-five occasions without embolism. In the post-mortem room puncture of the sac with a sharp trocar, whether performed slowly or quickly, obliquely or normally to the surface, causes no detachment of clot. The danger of embolism, therefore, may be disregarded until the contrary is shown. It is probably great when electrolysis is employed and the current reversed during the sitting.

¹ *Trans. Roy. Acad. Med. Irel.*, Dublin, 1911, xxix, p. 24.

The chief indications for the operation of wiring are: (1) An aneurysm of the ascending part of the arch of the aorta, especially if X-ray examination in two planes at right angles to each other indicates sacculatation. (2) Abdominal aneurysm in the usual situation—namely, at the origin of the cœliac axis. Both these types of aneurysm are usually saccular, and the louder the bruit the greater is the chance of a case being a suitable one for wiring, because the aneurysm is probably saccular and the opening of the sac small. Medical treatment is of no avail.

The chief contra-indications are: (1) Rapid increase of pain or of pressure symptoms. These are probably indicative of an early and fatal termination. If these symptoms pass away under treatment the question of operation can be again considered. (2) The presence of a second aneurysm. (3) Sepsis. (4) Involvement of the transverse part of the arch. The cases recorded by Hodgson show clearly that the patient's discomfort is much increased by consolidation taking place in this situation.

As regards the instruments, Nos. 1 and 2 are now obsolete. The advantages claimed for instrument No. 3—the one here shown—are: First, that asepsis is absolutely secured; secondly, that there is a minimal risk of wire entering the aorta; thirdly, that the operation can be performed easily, quickly and gently. It is important to emphasize the latter point, because the idea has become prevalent that force is needed. The whole secret of avoiding shock in this part of the operation seems to lie in pushing home the piston very gently. The record of cases just given shows that it is absolutely essential to see blood spurting through the cannula before the cartridge is inserted, for there is otherwise no certainty that the wires will open out in the sac or that they will enter the blood-stream at all. It is also advisable to withdraw the cannula until the end only just projects into the blood-stream, because if the wires, on emerging from the cannula, are close to the opposite wall of the sac they may not open out properly. Much damage might be done in this way, especially if any force were used. Fourthly, the exact quantity of wire is known and its probable arrangement in the sac may be assumed with some degree of accuracy. Lastly, the dull gilding of the wire provides a granular surface, as proved by Holt's case, which is most efficient in collecting firmly adherent fibrin from the blood.

MR. C. BRAINE-HARTNELL: The case I wish to mention is one of abdominal aneurysm presenting very unusual features, on which I

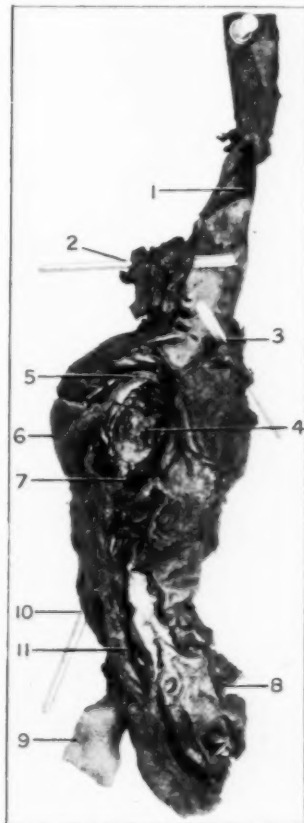
operated by the introduction of wire into the sac by means of Colt's apparatus. The patient, aged 41, was admitted to the General Hospital, Cheltenham, as a case of appendicitis; he was complaining of acute pain and had a rigid rectus muscle. The temperature was 100° F., and the pulse 66. There was no tenderness *per rectum*, and the leucocyte count was 8,000 on three separate examinations. The patient was transferred to the care of my colleague Dr. Collins for further observation, and it is entirely due to his thorough and repeated examinations that a diagnosis of abdominal aneurysm was made. The patient gave a history of loss of weight and obstinate constipation for the past twelve months. On March 26, 1912, he had his first attack of agonizing pain. He was admitted to hospital on April 2. On examination, the urine contained a few blood cells, the hæmoglobin was 100 per cent., the blood-pressure 115 mm. of mercury. The knee-jerks and pupil reflex were normal. The stomach was dilated. The least exertion, such as turning in bed, caused the most acute pain, which was scarcely controlled by morphia. A swelling could be made out in the right hypochondrium wholly to the right of the middle line. The tumour pulsated, but it was difficult to say whether or not the pulsation was expansile. A systolic murmur was heard over the swelling and along the spinal column. The right dorsalis pedis could not be felt, the left was normal. On April 6 he passed bright blood *per rectum*. On April 14 the right leg and foot became œdematous, but there was no œdema in the left until April 28. On April 14 the right epigastric vein was found distended, and small dilated venules were seen below the right costal arch. The temperature was irregularly febrile. Laxatives caused intense pain. Wassermann's reaction was negative; von Pirquet feebly positive. The tumour was much more palpable on some days than others.

The operation was performed on April 30. A rubber air-cushion was placed under the dorsal spines. The abdomen was opened from the ensiform cartilage to below the umbilicus. On passing the hand in, a large globular, pulsating swelling about 4½ in. in diameter, of the size of a large Jaffa orange, was found springing from the aorta and extending over to the right hypochondrium. The tumour reached from below the renal artery to the aortic bifurcation. It was extremely tense. The transverse colon and the duodenum were lying in front of it, the latter being very adherent to the wall of the sac. The external peritoneal reflection of the ascending colon was torn through, and the duodenum with difficulty separated from the sac, in an upward and inward direction. Colt's trocar was thrust into the aneurysm, and on removing the aspirator a jet of blood shot up for 2 ft. and blood welled up by the cannula.

A cage packing containing 150 in. of wire with a surface area of $3\frac{1}{2}$ sq. in. was passed into the tumour. On withdrawing the cannula there was free bleeding from the site of the puncture, which stopped after ten minutes' pressure with a gauze sponge. The abdomen was closed without a drain. There was considerable pain for twenty-four hours following the operation. There was frequent vomiting of dark green watery fluid, which continued until his death on May 6. A few hours after the operation the dorsalis pedis in the right foot could be felt. On the following day the left foot was more œdematous than the right, from which the œdema was fast disappearing. On May 3 all trace of œdema had disappeared from both feet. Auscultation on May 3 found the bruit to be coarser, and a definite bellows murmur. The patient died on May 6.

Post-mortem Report.—No peritonitis. The aneurysm extended from the right renal artery to the bifurcation of the aorta. The sac came off the right side of the aorta, and lay wholly to the right of the middle line. The external measurements of the aneurysm were $4\frac{1}{2}$ in. in length and 3 in. in breadth. There was an oval opening from the aorta into the aneurysm 2 in. by 1 in. on its right wall, filled with firm clots. There was a further opening on the left and lower extremity which dissected down outside to the bifurcation of the left common iliac, encircling three-quarters of its circumference. The superior end of the wire was found projecting through a point $\frac{3}{8}$ in. above the centre of the oval opening on the right side, having torn its way through the aortic wall. The inferior end of the wire was tucked away inside the aneurysm immediately outside the endothelium, which tore on handling the specimen. It was now seen that the wire had not opened into a cage form but was lying with the component wires close together embracing the anterior border of the opening into the aneurysm. The site of the puncture made by the trocar was $\frac{1}{2}$ in. behind the centre of the aneurysm. The vena cava lay immediately behind the aneurysm, and on slitting it up the union of the two iliacs occurred at the junction of the lower and upper three-fourths of the aneurysm. The way in which the aneurysm overhung the right iliac vein offered an explanation for the œdema of the right leg preceding that of the left in the course of the illness. Small patches of atheroma were present in the aorta and common iliac vessels. The transverse colon was lying over the upper half of the aneurysm. The left renal vein was seen running just above the superior border. The duodenum and pancreas were very closely adherent to the sac. It was interesting to note that in spite of the fact that the man suffered from intense pain,

there was no erosion of the vertebra, and we suggest that the pain was caused by the dissecting aneurysm along the left common iliac artery. The stomach was very dilated, its lower border reaching to the umbilicus.



Mr. Braine-Hartnell's case of Abdominal Aneurysm. 1, aorta; 2, coeliac axis; 3, left renal artery; 4, oval opening into aneurysm; 5, upper end of wire; 6, site of puncture for introduction of wire; 7, lower end of wire; 8, left common iliac artery; 9, right common iliac artery; 10, rod in inferior vena cava; 11, dissecting aneurysm.

As criticism on this method of treatment we submit the following:—

- (1) The wire did not form in a cage as it is supposed to do.
- (2) The wire that we used was too strong.
- (3) Too much wire was introduced.

Mr. CHARLES A. BALLANCE desired, in the first place, to thank Mr. Barling for the pleasure which he had derived from listening to his very admirable paper, and his admiration was much increased by the way in which it was delivered. He felt that he could understand and follow every argument he used, which was not the case with all the papers one listened to. There was no doubt that surgeons at the present day had very little experience of aneurysm compared with the experience of surgeons at the time when he was a student. Therefore, as he walked down the room he felt that it required considerable courage to bring forward a paper on the general treatment of aneurysm, and he could not help reflecting that it was as well that he was not doing so himself. But since he had listened to the paper he felt that he was wrong, and certainly the Section was greatly indebted to the opener for the trouble he had taken to bring the subject forward. He did not propose to relate the few cases which had come under his treatment; they were mostly cases of popliteal aneurysm such as all surgeons had treated. But what he proposed to do, briefly, was to try and discuss the principles on which the cure of aneurysm must be secured, if that cure were to be obtained at all.

Antonio Scarpa, who was surgeon at the Imperial and Royal University of Pavia at the beginning of the last century, wrote a small book, a copy of which was in the Library, on "Aneurysm and its Treatment," and these were the words from the book, as translated: "It is a certain and incontrovertible fact in practical surgery that a complete and radical cure of aneurysm cannot be obtained, in whatever part of the body this tumour is situated, unless the ulcerated, lacerated and wounded artery from which the aneurysm is derived is, by the assistance of Nature, or of Nature combined with Art, obliterated and converted into a perfectly solid ligamentous substance for a certain space above and below the place of ulceration, laceration, or wound." Some years ago he (the speaker) took a good deal of trouble to inspect aneurysms in the museums of this City and in other museums in England and abroad, and he was not able to find any specimen which controverted this great principle which was laid down by Antonio Scarpa, that the aneurysm could not be cured unless the artery was obliterated at the site of the aneurysm. There was, however, one specimen in Guy's Hospital Museum—which, unfortunately, was not among the present collection in that room—which was unique. That was a specimen which showed the external iliac artery completely obliterated in its whole extent from a ligature which was placed upon it by Sir Astley

Cooper. This ligature was placed upon the external iliac for the cure of a large femoral aneurysm. Suppuration occurred, and the aneurysm burst; clot and pus poured forth, and ultimately the man got well. The external iliac artery was obliterated, and on the common femoral artery at the site of aneurysm was a patch of fibrous tissue; and the femoral artery at this spot was apparently pervious. It could not have been pervious at the time the aneurysm suppurred and burst, otherwise the man would have bled to death. That was the only exception to Scarpa's law which he knew of previous to the work which Matas had done. The older surgeons really had three methods of treatment. One was the Hunterian method of ligature, and another Anel's method, which was not a modification of Hunter's method, because he operated upon the brachial artery; and it was well known that operations upon the arteries of the upper extremity could not be compared with operations on the arteries of the lower extremity. Besides the ligature there was the old operation for aneurysm—i.e., incision of the sac, turning out the clot, and ligaturing the artery above and below the aneurysm. John Hunter said that in his day every case of popliteal aneurysm treated by the "old operation for aneurysm" was a failure, for the operation always resulted in gangrene, and this was followed by amputation and death. Besides those methods, which were still practised, there was another, a modern method which had been made possible by the enormous advances which the work of Lord Lister had made possible in surgical practice. He referred to excision of an aneurysm. He (Mr. Ballance) thought excision of the aneurysm was the ideal treatment, but obviously in many cases excision was impossible. The old operation of Antyllus of turning out the clot and tying the artery above and below was very fatal. He thought Matas's obliteration method was a modern extension of the old operation of Antyllus. The obliterative operation was the proper one to carry out when it was desirable to incise the sac of an aneurysm. He was present at the meeting of the American Medical Association a few years ago, in 1906 or 1907, when it met at Boston, and there he had the pleasure of meeting Dr. Matas and talking the question over with him. He had an immense admiration for the work of Dr. Matas, but it should be remembered that without the wonderful work of Carrel and Guthrie on the suture of the arteries it would hardly have been possible for Dr. Matas to have opened a discussion on his method of treatment of aneurysm in one of the theatres in Boston. He (Mr. Ballance) thought he would be in time for the meeting if he arrived half an

hour before it was advertised to take place. But American surgeons were so interested in the subject that when he arrived the only place for him was standing room in the top gallery. He had been asked to take part in the discussion, but as no one could find him in the top gallery, he escaped that pleasure. Afterwards, on several occasions he had the opportunity of talking to Dr. Matas about the beautiful methods which he had introduced for the treatment of aneurysm. Dr. Matas was very enthusiastic about the obliterative method, and that method really was founded upon the great principle which was first enunciated by Antonio Scarpa, that the artery must be obliterated at the site of the aneurysm if the aneurysm was to be cured. The other method, the reconstruction of the artery on the other side of the aneurysm, Dr. Matas was not so enthusiastic about, but said only occasionally was it possible to do it, and he thought that in future almost all his operations would be procedures for obliterating the artery and the sac of the aneurysm. That he (Mr. Ballance) thought was an extremely interesting matter, because he believed in the doctrine of Scarpa, and he believed it was only very occasionally that surgeons would be able in future to cure an aneurysm and also re-establish the circulation through the artery at the site of the aneurysm. In reference to the statements of Dr. Matas with regard to the re-establishment of the circulation, Dr. Matas told him it was re-established at the time of the operation, but that of course he could not be sure that it was permanently re-established; he could not be certain that the blood continued to flow at the site of the aneurysm, and he (Mr. Ballance) did not think one should come to any scientific conclusion on that point, or could do so, unless the actual specimens illustrating that result were shown. Therefore he would be very doubtful about the reconstruction of the artery behind an aneurysm in the case of the popliteal or any other artery, and he thought that, in most cases, the artery became obliterated as well as the aneurysm, perhaps some time after the reconstruction operation took place.

What was the result of treatment by the Hunterian method of ligation? Did surgeons want to do a difficult dissection in the presence of a great pulsating tumour in the popliteal space when a cure could be obtained by a simpler method? In 1890 Sir Anthony Bowlby published an article on the subject¹ and referred to a paper read before the Royal Medico-Chirurgical Society in 1887 by Sir William Savory² as supporting his view. He recommended, because certain cases had had recurrent

¹ *Brit. Med. Journ.*, 1890, ii, p. 1237.

² *Med. Chir. Trans.*, 1887, lxx, pp. 139-47.

pulsation, that the artery in future should be ligatured at the upper part of the popliteal space. For his (Mr. Ballance's) part, he did not think those authors proved their case, but the paper was of extreme interest, and it had been in his mind ever since. They related 23 cases of popliteal aneurysm treated by Hunterian ligature during the previous ten years at St. Bartholomew's Hospital. Sixteen of those cases were immediately and permanently cured; 4 had impending gangrene when they came into the Hospital, and all surgeons had probably seen those cases. No treatment could possibly save such a limb from becoming completely gangrenous. In those 4 cases amputation was necessary. He thought 4 cases out of 23 requiring amputation for gangrene was about the usual proportion in popliteal aneurysm—certainly in London hospitals. There were 3 cases of the 23 in which pulsation recurred. Two of those were cured by a short rest in bed, so those two could be added to the others—e.g., 18 cases successfully treated by Hunterian ligature. The third case of recurrent pulsation was treated by ligature of the popliteal artery in the upper part of the popliteal space, that is, between the site of the first ligature and the aneurysm. And that patient was cured. So they were all cured except the four with gangrene, which had amputation done; a wonderful result. And it had always appeared to him that while such splendid results could be obtained there was no need to try to find out a better method of treatment of aneurysm in the popliteal space. He felt confident that Dr. Matas's method could not show better results in the popliteal space, nor even so good as those reported in this paper. With regard to aneurysm of other arteries, which one could not very well treat by the Hunterian ligature, or at all, he thought Matas's obliterative method was certainly a splendid one. And possibly it might be applied to the abdominal aorta, or even the thoracic aorta, especially as it had been shown by Professor Halsted, of Baltimore, that the thoracic aorta in dogs could be successfully obliterated. But with Matas's method the aorta would not require obliteration, the aneurysm only being sewn up. He had not time to mention other methods of treating aneurysm, but he wished to defend the Hunterian method for the treatment of popliteal aneurysm. He could not say how many times he had tied the femoral artery for aneurysm, but at the present time he had not had a failure, nor a case of gangrene, the reason being that the number of cases he had had was so small. There was one point about the ligature which he would like to refer to. Mr. Barling spoke about the use of two ligatures, one ligature applied first, and then another afterwards. That really was the method of that great surgeon Nicholas Senn. The

application of the "stay-knot" which Mr. Edmunds and he proposed some years ago was different. Both ligatures were applied together. The friction between the two loops and the two first hitches prevented the expansion of the loops by the pressure of the blood during the tying of the second hitches of the reef-knots. Thus, when the stay-knot was completed there was no chance of the artery being in any way patent at the site of ligature. This was the principle involved in the employment of the stay-knot.

Mr. CHARTERS SYMONDS agreed very distinctly with the position taken up by Mr. Ballance. He felt that the development of the treatment of aneurysm by obliteration was applicable to aneurysms in certain situations. With regard to the popliteal, he agreed with Mr. Ballance that when so great a success had followed the ligature of the superficial femoral, it was rather risky surgery to embark upon dangerous proceedings in the popliteal space. He agreed with Mr. Ballance that such methods as excision and obliteration should not be applied to such an aneurysm as that of the popliteal, but that they should be reserved for aneurysms especially of the first part of the axillary and the third part of the subclavian for choice. It seemed to him that those methods could be used in those situations. The two cases referred to by Mr. Barling as having occurred in this country were aneurysms excised from the third part of the subclavian. He believed the first was done by the younger Mr. Allingham, a very brilliant operation, and that the second one was at Carlisle. Both were successful, and in both there was resection of the clavicle. It had been proved that a man could work well without his clavicle. In those situations there was a very fair field for operation by this particular method. With regard to the treatment by the introduction of wire, &c., he only once carried that method out—namely, in an aneurysm of the abdominal aorta. The patient was afterwards shown at a meeting of the Medical Society of London. The man came to hospital with symptoms pointing to duodenal ulcer. Being uncertain about the condition, he was sent away, and later he returned with aneurysm. No difficulty was encountered, and several feet of aluminium-bronze wire were put in, and there was no subsequent trouble. That was a form of aneurysm which he hoped might be treated by the methods described by Mr. Barling on this occasion. The introduction of wire had not generally proved very successful. In his own case it did very little good, though fortunately it did no harm. With regard to aneurysms at the root of the neck, the subject should be divided up according to regions. He had carried out distal ligature on

more than one occasion, and in the last case with so much success in an aortic aneurysm that the man was able to return to his work as an engine-fitter. Subsequently he died from extension of the aneurysm. He did not propose to refer to the details as to material used; his object had been principally to join with Mr. Ballance in saying that, in reference to the common aneurysm—namely, that in the popliteal space—his view was they had a very safe and successful method in the Hunterian ligature.

Mr. ARTHUR BARKER said he would gladly contribute the only case of operation by Matas's method which he had had. There had only been two at University College Hospital, one of which was done by himself. Whatever might be said of the operation, it was not a difficult one; in fact it struck him as being singularly easy. The case was briefly as follows¹: The patient was a woman, aged 50, who had obviously had extensive syphilis. Her aneurysm was a large sacculated one in the popliteal space. The artery was controlled by an elastic bandage, and the sac laid open freely and the clot turned out. Then the orifices of both the proximal and distal parts of the artery were found and sutured from within. The aneurysm sac was folded in, in the way described by Mr. Barling. The only other point of interest was that the vein was already obliterated, and that made him somewhat uneasy. But probably because the obliteration had been gradual, other veins had taken on a share of the work of the obliterated vessel. The aneurysm folded together easily. He used simple linen thread sutures, and everything went smoothly, union being flawless, and the patient soon walked about. The other case was, he believed, one of aneurysm of the external iliac, which was done similarly by one of his colleagues. That operation also was found to be easy, and it went very well. He did not consider that the difficulty was greater than was met with in securing an artery by the Hunterian method. All surgeons had suffered in a way, surgically, from the rarity of these conditions nowadays, and medical officers in the Army said that they now saw few or none. His own experience of popliteal aneurysm had been much the same as Mr. Lockwood's—i.e., he had not seen many, perhaps six or eight. They had been treated in various ways, including ligature by the Hunterian method. Two were cured by digital compression. One cure of aneurysm struck him as remarkable. The case had been published. It was that of a man of large size who had a tumour in his left iliac fossa, and it looked as if it

¹ *Brit. Med. Journ.*, 1911, ii, p. 102.

were about to burst, so violently was it pulsating. He begged for something to be done. Digital compression higher up was tried, but the patient could not stand it. His colleagues had been examining the patient just before he was put on the table, and they thought it was a dangerous case to tackle. The effect of the chloroform was to agitate him very much, and there was an increase in the violence of pulsation. He had to wait for some time before approaching it with the knife. He had made his first skin incision and was just mopping up the blood, when the aneurysm was found to be consolidated. A colleague said, "Why do you not go on?" He replied that it was solid. It remained solid and was cured. The man came in again five or six years afterwards with an aortic aneurysm, of which he died. The specimen, now in University College Museum, shows that the iliac aneurysm referred to had been quite cured. That would give one some encouragement in trying to treat these cases without operation, because though the man's scar was there he had not really opened the abdomen at all. He had cured several popliteal aneurysms by simple digital compression in a short time, and it was possible that such measures as these were being neglected at the present day. He would be grateful if anyone present could suggest what ought to be done in a patient at present under his care with an aneurysm of the left subclavian extending from the first stage of the artery to just below the second rib. He had kept the patient quiet in bed for months, and as a result he had lost the intense pain which he had at first, and which kept him awake at night. He had also been having iodide of potassium, and was looking better than he did. But the aneurysm had not diminished in size, and the question now was what to do? If any advice could be offered him he would be glad.

Mr. GILBERT BARLING, in reply, thanked all who had taken part in the discussion for the kind way in which they had received his rather poor efforts in discussing a subject on which he had not very much material. He would have liked to have been able to look carefully through all the specimens which had been got together in the room, to see which would lend themselves to an operation which he regarded as ideal, as opposed to any other method. A method to be ideal must be one which, while curing the aneurysm yet allowed the blood-current to flow. Whether such was attainable was another matter. He was not prepared to say that, given any aneurysm, he would adopt Matas's operation; it was best to keep an open mind, and select for each case the procedure most proper. He would have liked to have performed restoration in the little internal carotid aneurysm, but he

thought he might fail if he did, and of course the safety of the patient was the great consideration. Nothing seemed to have transpired in the discussion which it was necessary for him to attempt to refute. He agreed with nearly everything which had been said concerning popliteal aneurysm. Surgeons had now a very good method, but he remembered that his first case suffered from gangrene, which was unfortunate. If he had obliterated it by Matas's method, he wondered whether he would have avoided gangrene. The patient's circulation would have been interrupted less, or embarrassed less, and the gangrene might have been obviated. He had never tried the introduction of wire, but he had tried electrolysis, and had been deeply disappointed with it, so that he was not likely to try it again. He had tried the operation of needling, but he did not think the patient was either better or worse, and he was disappointed at the absence of improvement.

Exhibition of Aneurysms.

DURING the two days immediately preceding the debate, a magnificent exhibition was held of 190 museum specimens of aneurysms of all varieties selected by Mr. James Berry, and kindly lent by the curators of the Metropolitan museums. Among the specimens of unusual interest were the following:—

Aneurysm of the descending aorta of a foetus. (London Hospital.)

Dilated pulmonary artery simulating aortic aneurysm. The left common carotid artery had been tied with apparent benefit. Years afterwards the patient died of phthisis, and it was then found that there had been nothing the matter with the aorta. (St. George's Hospital.)

Dissecting aneurysm of the transverse and descending aorta. (St. Bartholomew's Hospital.)

Aneurysm of the arch of the aorta, the existence of which had not been suspected during life, the patient, an old man, dying of disease of the kidneys. (University College Hospital.)

Aneurysm of the sinus of Valsalva rupturing into the left ventricle. (London Temperance Hospital.)

Multiple aneurysms of the aorta. (Westminster Hospital.)

Aneurysms of the aorta eroding the sternum and ribs and forming large secondary cavities in the front of the chest and back respectively. (Royal Free Hospital and Middlesex Hospital.)

Murchison and Moore's historic specimen of aortic aneurysm treated in 1864 by the introduction of iron wire. (Middlesex Hospital.)

Aneurysm of the innominate cured by venesection performed forty-two times between October, 1824, and June, 1827. (London Hospital.)

Calcified intracranial aneurysm. (St. Bartholomew's Hospital.)

Aneurysm of internal carotid artery as large as a tangerine orange successfully treated by excision. (University College Hospital.)

Aneurysm of the internal carotid in a girl, aged 3, which had followed the opening of a tonsillar abscess. Four weeks later the aneurysm ruptured into the pharynx with fatal result. (Westminster Hospital.)

Cirroid aneurysm of the temporal. (King's College Hospital.)

Aneurysm of subclavian successfully removed by excision after previous ineffectual ligature of the subclavian artery. (St. George's Hospital.)

Arterio-venous aneurysm of the arm, treated by amputation. (Charing Cross Hospital.)

Aneurysm of abdominal aorta rupturing into the mesentery. (Guy's Hospital.)

Aneurysm of abdominal aorta opening into the left common iliac vein and shutting off all communication between that vein and the vena cava. (St. Thomas's Hospital.)

Arterio-venous aneurysm of the splenic vessels. (Guy's Hospital.)

Aneurysm of the gastro-epiploic (Guy's Hospital) and splenic. (London Hospital and Guy's Hospital.)

Femoral aneurysm cured by pressure by Liston in 1844, one of the first cases of the kind in this country. (University College Hospital.)

A double femoral artery, only one of which had been tied (unsuccessfully) for popliteal aneurysm. (University College Hospital.)

Double popliteal aneurysms cured by ligature of both femoral arteries. (Guy's Hospital.)

Popliteal aneurysm from an old gentleman, aged 90. It had been cured by the gentle pressure of a bandage. (St. George's Hospital.)

Popliteal aneurysm treated by ligature of femoral artery with silver wire. (St. George's Hospital.)

Numerous other specimens of popliteal aneurysm from St. Mary's and nearly all the other hospitals already mentioned.

Aneurysms of the profunda (Guy's Hospital) and dorsalis pedis (St. Thomas's Hospital).

Surgical Section.

June 11, 1912.

Mr. CLINTON T. DENT, President of the Section, in the Chair.

Cases of Intractable Constipation treated by Operation.

By P. LOCKHART MUMMERY, F.R.C.S.

CONSTIPATION of a more or less serious character is a very common condition, probably one of the commonest for which patients consult their medical advisers. The surgeon is only called in for cases where the condition has reached an extreme degree, and then only as a rule after the patient has been under medical treatment for years. It is only after all the ordinary, and often extraordinary, methods of treatment have failed that the aid of surgery is invoked.

Although it has become usual to speak of chronic constipation as a disease, it is nevertheless only a symptom common to a great number of totally distinct and separate affections. Chronic constipation, like many other complaints, is in most cases a result of modern civilization and dietary, and is one of the penalties we pay for living on prepared foods.

As constipation is not a disease it can have no distinctive pathology; we can, however, recognize three distinct types:—

(1) Obstructive constipation, in which some definite obstruction exists to the passage of faecal material along the colon.

(2) Atonic constipation, in which the peristaltic and expulsive power of the colon is deficient.

(3) Undue solidity of the faecal material interfering with its passage along the colon.

Undue retention of faecal material within the body is not itself of importance. It is rather the results of this retention which cause trouble, and for the prevention of which surgical treatment is sometimes sought.

Of the extremely poisonous nature of the toxins which are produced in the bowel as the result of the retention of faecal material in the colon we have good evidence in cases of intestinal obstruction. Where acute intestinal obstruction occurs the cause of death is almost without exception a profound toxæmia rather than any direct result of the obstruction. Nesbitt, who produced intestinal obstruction artificially in dogs, found that highly poisonous substances were formed in the occluded loops of bowel. The most notable of these were neurin and cholin. Clairmont and Ranzi found by experiment that while the filtrate from the contents of the normal intestine produced no harmful effects when injected into animals, a similar filtrate prepared from the contents of a loop of strangulated bowel produced serious, and often fatal, results when injected.

The toxæmia in chronic constipation is never so serious as in cases of intestinal obstruction because the poisoning occurs more slowly, and, the bowel wall being undamaged, absorption also occurs more slowly. In time, however, the constant slow poisoning which results from chronic faecal accumulation causes very serious symptoms. One of the most marked of these is a progressive loss of weight. The patient loses most of the natural fat, with the result that the skin becomes loose, and the abdominal organs, which are largely dependent upon their surrounding fat for the maintenance of their normal positions, become loose, and a marked degree of visceroptosis results which still further aggravates the original condition. Discoloration of the skin is another characteristic symptom in bad cases. Usually the skin becomes a dull earthy colour, while in a few cases I have seen large patches of brown discoloration which caused considerable disfigurement. Other symptoms, such as headache, neuralgia, sleeplessness, loss of appetite, and general lack of vitality are too well known to warrant further mention. Not infrequently the most serious aspect of the case is the mental depression which accompanies the toxæmia. I have known patients who threatened to commit suicide, and doubtless everyone has met with similar cases.

While these symptoms are the rule in bad cases, it is a curious and well-known fact that some persons appear to be quite immune from the results of faecal retention. Most of us have probably met with patients who suffer severely from constipation, almost to the extent of getting obstruction, and yet never suffer from symptoms of auto-intoxication. I have seen more than one patient who had not had an action of the bowels for over a month, and yet was in excellent health. Such cases are well known, and we must assume either that the poisons are not absorbed or that the patient is immune to their effects.

I do not propose to embark here on the various theories respecting the mechanism causing many of these cases of constipation. There has, I think, been too much theorizing and too little practical pathology. Nor do I propose to discuss the question of theoretical kinks which can be demonstrated by X-rays. I shall confine my remarks almost entirely to those cases which have come directly under my own observation, and in which the actual lesion causing obstruction of the bowel was demonstrated. It is only by careful study of cases in which a definite lesion is demonstrable that we can arrive at the truth.

The cases of severe constipation which are brought to the surgeon may be conveniently divided into two classes. Cases of obstructive constipation form the majority of them, and the minority is made up of cases of atonic constipation. I propose to deal with these in detail, illustrating my remarks from cases which have been under my care, of which I have made a tabulated list.

CASES OF OBSTRUCTIVE CONSTIPATION.

These form the majority of the cases brought to the surgeon and are those which, in most instances, can only be treated successfully by surgical operation. Operations which are performed for chronic constipation without reference to the underlying pathological cause cannot be considered as satisfactory or scientific procedures, and our greatest difficulty is to be able to make a correct diagnosis, or even working hypothesis, as to the cause of the faecal delay. The diagnosis is often made possible by a sigmoidoscopic examination after the bowel has been well emptied by enemata, and I have found this by far the most valuable aid to diagnosis in these cases. The presence of adhesions involving the pelvic colon and kinking it, is readily diagnosed by means of the sigmoidoscope. As a result of using it I have frequently been able to state that the sigmoid was bound down into the iliac fossa by adhesions; and this diagnosis having been in many cases completely confirmed by a subsequent laparotomy, I have gained considerable confidence in diagnosing adhesions in this manner.

X-ray photographs after a bismuth meal or after large enemata of bismuth emulsion will sometimes afford valuable information; but I think we should accept the evidence of these photographs, like all X-ray evidence, with caution. They are of value as confirmatory evidence, but a diagnosis should, in my opinion, never be founded upon X-ray photographs alone, and I have very little faith in the diagnosis of kinks

from X-ray appearances when there is not sigmoidoscopic or other evidence to confirm the diagnosis. They are particularly useful in showing strictures such as those seen in pericolicitis and in cases of ptosis of the transverse colon.

It is obvious that there must normally be a very large number of kinks in the alimentary canal, or it would be impossible to pack nearly 40 ft. of it into the abdominal cavity. A kink in the bowel is of absolutely no importance as long as the bowel retains a reasonable amount of mobility, the kinks straightening out as the contents pass along. A kink can only produce partial obstruction when, owing to adhesions or some other cause, the bowel is so fixed that the kink cannot be straightened out.

It is obvious that by the X-rays it is quite impossible to tell the difference between a normal kink and one due to adhesions. The so-called iliac kink, about which we have recently heard a good deal, is, I think, open to grave suspicion as a pathological cause of constipation. Food naturally accumulates in the terminal coils of the small bowel lying in the pelvis, and there must be a kink in the ileum where it joins the more fixed cæcum. The X-ray appearances show a considerable amount of food in the terminal portion of the ileum, and a kink between this portion and the cæcum. I see nothing, however, to oppose the view that this is a normal state.

I also think that observations upon the rate of passage of a bismuth meal should be accepted with great caution as proving anything. There can be no question that observations of this nature made by Dr. Hertz and others have been of great value in acquainting us with the normal manner in which the food passes through the alimentary canal. But when it is attempted to prove constipation by this method it is advisable to be very cautious. In the first place, bismuth in large doses is one of the best known drugs for producing constipation, or, in other words, for stopping diarrhœa. Again, bismuth, like other drugs, varies greatly in its effect upon different individuals, and thereby a serious error is brought into the investigation. Moreover, it is not correct to argue that because delay occurs in the passage of the test meal along the ascending colon the obstruction is just in front of it. It would be as correct to argue that the cause of a train being late in leaving Victoria Station was an obstruction just outside the station, when it is just as likely to be a breakdown at the Brighton end of the line.

CAUSES OF OBSTRUCTIVE CONSTIPATION.

Adhesions.

This was one of the commonest causes in my series, being present in eight out of the total. Adhesions usually cause chronic obstruction by producing a kink in the bowel which interferes with the passage of anything but fluid fæces along its lumen. When adhesions directly constrict the bowel, as in the case of the formation of a band, the obstruction caused is usually acute. The best description of the different varieties of adhesions involving the bowel is to be found in the article on intestinal obstruction, written by the late Mr. Barnard, in Clifford Allbutt's "System of Medicine."¹ Dr. Tuttle, of New York, has also described a number of cases.²

Cases due to adhesions are generally characterized by well-localized pain in the abdomen, which is especially noticed at the time when peristalsis is active, that is to say, two or three hours after a meal and before the bowels act. The pain, in a few cases, is very severe, and is then probably the result of enterospasm in the section of bowel just above the kink. The worst adhesions were met with in patients who had suffered previously from localized peritonitis or who had had previous abdominal operations. Localized bands of adhesions could, in a few cases, be traced to some definite cause as, for instance, an attack of typhoid fever, inflamed glands, perimetritis, &c. In quite a number of cases, however, in which well-marked bands of adhesions were found, no cause could be discovered. The cause of these adhesions is often very obscure. We know that in some patients adhesions form readily and persist for years, even increasing apparently in length and toughness. In other patients, however, adhesions known to be present rapidly disappear and leave apparently no trace behind.

When a patient recovers from an attack of general or localized peritonitis very extensive adhesions must be left, but there are many well-authenticated cases where a subsequent operation on the abdomen for some other cause has demonstrated the complete absence of any adhesions. I have recorded two cases in my book on "Diseases of the Colon," in which patients suffering from acute volvulus had a temporary colotomy performed in order to drain the loop after untwisting the volvulus, and yet, in both cases, the volvulus recurred after intervals of

¹ Allbutt and Rolleston, "System of Medicine," 1907, iii, pp. 704-810.

² *New York Med. Journ.*, 1908, lxxxvii, pp. 479-86.

one and two years respectively, and at the operations no trace of the fixation to the abdominal wall was discovered.

Some of the cases in which adhesions have occurred after apparently aseptic operations upon the abdomen are probably due to blood clot left in the abdomen. In this connexion I might quote Baisch's experiments upon animals.¹

He performed two series of experiments, in both of which similar peritoneal lesions were produced. In one series complete hæmostasis was secured, and in the other varying quantities of blood were allowed to remain in the abdomen. In the first series he found subsequently that no adhesions had developed, while in the second they were constantly present.

Operative treatment is the only thing which offers any probability of permanent cure in those cases of partial obstruction due to adhesions. In the past there have been many instances in which the adhesions, after division, have promptly recurred, and the patient has only been given very temporary relief. So much has this been the case that some surgeons have expressed the opinion that it is useless to operate as the patient may be made worse instead of better; while other surgeons have tried using thin sheets of gold, painting the surfaces with gum, glucose, or other substances to prevent the re-formation of adhesions. Nevertheless, most excellent and permanent results can be obtained by operation; but two factors are, in my opinion, absolutely necessary to a successful result. All raw surfaces left by division of the adhesions must be completely covered in, so as to leave no raw surface uncovered by peritoneum, and the most absolute asepticity and hæmostasis are a *sine qua non*. Further, great care must be taken to prevent any—even the most superficial—damage to the peritoneum.

If the adhesions are divided carefully, keeping in mind the necessity for closing in the raw surface, it is generally possible to close in the exposed area by stitching up the gap in the opposite direction. If not, a little freeing of the peritoneum by blunt dissection, or by the formation of peritoneal flaps, will enable it to be done quite easily. It is necessary to exercise the greatest care to avoid cutting any of the small vessels just under the peritoneum, as bleeding is difficult to stop entirely, and blood clot will ruin the result. I generally do the stitching with fine round-bodied needles, preferably straight, using a continuous mattress stitch and being careful to bury the knots and to

¹ *Beitr. z. Geburtsh. u. Gynäk.*, Berlin, 1905, ix, pp. 437-80.

leave the line of incision so that no thread can be seen anywhere. At first I used fine catgut, but I have now discarded this in favour of sewing cotton. It is difficult to get catgut sufficiently fine which will not break, and moreover, it is not so easy to manipulate as thread. I always take care to prevent the thread touching the skin, or, in fact, anything but the peritoneum, during the process of sewing, and I use sterilized batiste clipped to the edges of the wound in the abdominal wall.

The first knot should be tied on the underside of the peritoneum so that it will lie outside the peritoneal cavity. The finishing knot can be tucked in behind the line of suture, and if fine cotton thread is used, these knots are very small. Antiseptics should not be used in such a way that any chemical solution can come in contact with the peritoneum. I prefer to have the instruments on a dry towel, and to use dry swabs wrung out of normal salt solution. I always wear rubber gloves, and avoid handling the parts more than is absolutely necessary.

When the adhesions are extensive it is, of course, impossible to close in all the raw surface, and such cases are, as a rule, very unsatisfactory to treat. The worst bands can, however, sometimes be treated in this way with considerable relief to the patient. I have obtained the best results in those cases where a single band of adhesions existed. The presence of extensive adhesions in the peritoneal cavity renders it, as a rule, impossible to obtain a perfect result. Often the best procedure will be to short-circuit the coil of intestine which is most involved, so as to provide another and less obstructed path for the faecal contents. Each case, however, has to be treated on its merits. But one has always to bear in mind that any extensive separation of adhesions, or prolonged operation, will, owing to the fact that it involves much handling and traumatism of the peritoneum, almost certainly do more harm than good as regards the ultimate result.

In Case XVII I found there was no possibility of separating the adhesions, and I performed appendicostomy with the object of enabling the patient to wash out the colon and prevent the accumulation of hard masses within it. As was to be expected, the operation did not cure the patient, for she still had pain; but it greatly relieved her, and she put on weight and was able to get about better than before. Nearly two years afterwards she stated that she had undoubtedly obtained benefit from the operation.

Some of my best results have been in cases of adhesions, and as most of them have been in private patients I have been able to check the

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results. In the majority of them the condition of the patient is known from one to three years after the operation.

In five cases the result was all that could be desired a year or more after the operation, the patients describing themselves as cured. In two cases the results were very good, the patients being no longer invalided and the bowels acting regularly without trouble; but the patients still complained of minor symptoms, possibly due to adhesions. Both these patients were neurotic. In one case the result was unsatisfactory. This was a case of extensive adhesions, and appendicostomy was performed.

The essential factors which make for success in operations for localized adhesions are, I believe:—

- (1) Perfect asepsis.
- (2) Doing the operation bloodlessly, and particularly leaving no blood in the peritoneal cavity.
- (3) Covering in all raw surfaces and stumps by careful suturing, and, where necessary, by plastic operations on the peritoneum.
- (4) Gentle handling of the peritoneum.

Stricture.

There were seven cases of stricture in my series, and in all of them the stricture was due to pericolicitis. In five the pericolicitis was the ordinary simple form due to diverticulæ of the colon, and in two it was tuberculous in origin. In the cases due to diverticulitis the patients' ages were 62, 53, 46, 53 and 45, and the stricture was in the sigmoid flexure. In all it was a long tubular stricture and caused increasing constipation, in several cases dating back for some years, with occasional pain. A palpable tumour was detectable in all on careful examination. Two of the cases were thought to be malignant in character, but subsequently proved to be simple pericolicitis. In the other five the diagnosis was correctly made.

I do not propose to go into the differential diagnosis of this interesting condition, as it would take too long. I would only say that the sigmoidoscope and X-rays were the chief aids in making a correct diagnosis.

This condition is of particular interest in that it is often mistaken for inoperable malignant disease and accounts, I believe, for many of the cases of supposed cancer of the bowel which recover after colotomy.

Both the tuberculous cases were hyperplastic tubercle. One was in

a lady, aged 26, in whom the sigmoid was affected (this case has already been reported to the Clinical Section of this Society)¹ and the other in a child, aged 7, in whom the cæcal angle was affected.

In three cases the stricture was successfully resected, in two cases by myself, and in one by another surgeon. In one case colotomy was performed; in two the stricture was short-circuited; and in one no operation was done. All of these seven patients are at the present time in good health.

Foreign Body.

There was one case of foreign body. This was a particularly interesting case. The patient had suffered for about a year from increasing difficulty with the bowels, and an examination revealed a hard tumour, about the size and consistency of a fives ball, in the pelvic colon. I supposed this to be a malignant growth, but on opening the abdomen found it was a foreign body. It was removed from the colon through an incision and proved to be a faecal concretion largely composed of hair. The patient got quite well.

Congenital Dilatation.

There was one case of congenital dilatation of the colon in a gentleman, aged 23. He had suffered most severely from chronic constipation all his life, and an examination revealed the fact that his pelvic colon was 9 in. in diameter and occupied two-thirds of his abdominal cavity. It was not deemed justifiable to put the patient to the risk involved in the removal of such an enormous colon, and I performed appendicostomy with the object of enabling him more readily to prevent accumulation in the dilated sac. This was nearly three years ago, and he has been able since then to avoid any serious trouble with his bowels; though I have not recently had the opportunity of examining him, and, consequently do not know if there has been any diminution in the size of the dilated colon.

Kinks or Volvulus.

There are two of these cases in my series. One was in a young man, aged 29, and the other in a lady, aged 40. In both there was a very long mesentery to the pelvic colon, and this portion of the bowel normally

¹ *Proc. Roy. Soc. Med.*, 1910, iii (Clin. Sect.), p. 201.

assumed a position in which it was half twisted and faeces only passed with the greatest difficulty. Ordinary aperients were quite useless, and the patients were only able to get relief with large enemata, which had frequently to be repeated. In both cases the history of severe constipation dated back to infancy, and it seemed probable that the condition was congenital. In both I shortened the meso-sigmoid by rows of Lembert stitches inserted on the outer side with the object of preventing the recurrence of the volvulus. In neither case was the result entirely satisfactory. There was complete relief for some time in both cases, but after some months the old symptoms partly recurred, and I believe the mesentery again lengthened and allowed the volvulus to re-form. In another case of the same kind I should resect the sigmoid and perform an end-to-end anastomosis, so as to prevent any possibility of a recurrence of the volvulus.

Visceroptosis and Atony of the Bowel.

These two conditions are, in my experience, so commonly associated that it is most convenient to class them together. Of all the cases in my series these were by far the least satisfactory. There were eight of them altogether, and, with one exception, the patients were all women, most of them of a highly neurotic type, between the ages of 30 and 45. The symptoms in all were very severe. There was a serious degree of auto-intoxication—almost complete invalidism; the bowels refused to act except as the result of the most drastic measures, and the patients had tried almost every imaginable treatment short of operation. Both the patients themselves and their medical attendants were very anxious that something should be done. In all these cases aperients usually failed to produce any action of the bowels, even such drastic purges as 2 oz. of castor oil or two colocynth pills failing to relieve the bowels, and an action was only possible after repeated large enemata.

The degree of visceroptosis present was very severe. In most of the cases the transverse colon, and in some the lower part of the stomach, were pelvic organs. Almost everything in the abdomen had slipped down, and one was surprised that any of the abdominal organs functioned properly. One patient was X-rayed after a flexible metal bougie had been passed into the stomach, and the apex of the bougie was seen to lie behind the symphysis pubis. In all the cases the colon itself was much sacculated and its walls were very thin. Curiously enough, there was no marked weakness of the abdominal wall in most of the cases, while in

several the abdominal muscles were quite up to the normal. Certainly in none of my cases could one say that the visceroptosis was secondary to weakness of the abdominal walls. I do not believe the serious delay in the passage of the food residues through the colon which occurs in these cases is due to the abnormal position of the colon or to any increase in the flexures at the hepatic and splenic angles, as has often been suggested, but I think it is due to a general loss of tone in the muscular walls of the colon itself. We are at present very much in the dark as to exactly how or why this occurs.

One sees women with loose pendulous abdominal walls who have marked visceroptosis and yet have comparatively little difficulty in getting their bowels to act. The wearing of a properly fitting belt as a rule makes these patients quite comfortable and relieves their symptoms. The seven cases in my list, however, are of quite a different type. They were most of them women who had not had children, and there was no marked weakness of the abdominal wall in any of them. There seemed to be no satisfactory explanation why they should have developed visceroptosis. Two of them were under 32 years of age, and one was only 19, and yet they had severe visceroptosis with thin atonic sacculated colons; and medical treatment had entirely failed to get rid of their symptoms.

These cases strike me as very curious, and I have never met with anything quite similar in men. So far as my experience goes there is no surgical treatment which can be depended upon to cure them, unless a definite band of adhesions producing a kink or a chronic volvulus is discovered which can be directly treated. Appendicostomy, by enabling the bowel to be kept empty, gets rid of the auto-intoxication which is one of the most serious symptoms, and therefore gives considerable relief; but I cannot say that it entirely cures the patient, and two of my patients are not able to dispense with the opening after the lapse of three years in one case and one and a half years in the other. I think there is still a great deal to be discovered as to the exact pathology of these curious cases.

Case VIII is of considerable interest, partly because such severe atonic constipation is, in my experience, very rare in men, and partly because of the excellent results which followed appendicostomy. This was one of the worst cases of auto-intoxication I have ever seen, and the patient was thought to be dying. He was extremely emaciated, and his skin was of that peculiar shade that one is accustomed to associate with severe auto-intoxication. At the operation his colon was

found to be much dilated and very thin; there appeared to be hardly any muscular tissue in it. After the operation he improved in health in a quite extraordinary manner. The appendicostomy opening was closed eighteen months after the operation, and at the present time his physical appearance compares favourably with that of most men of his age.

Pressure upon the Bowel from outside.

There were only two instances of this in my series. In one (Case XXII) the constipation, which at the time I first saw the patient was the only thing complained of, was due to a large papillomatous cyst of the left ovary which pressed upon the pelvic colon, and by its weight prevented the passage of anything but liquid through it. Examination revealed the presence of the tumour, and after its removal the patient's bowels again acted in a normal manner. The patient is now quite well eighteen months after the operation. In the other case (Case XVIII) there was a rather enlarged and retroflexed uterus which practically blocked the posterior pelvic outlet. The fundus of the uterus could be felt just within the rectum and acted like a ball valve, almost completely preventing the passage of faeces. Relief could only be obtained by enemata and long tubes which temporarily pushed up the uterine fundus. The uterus, moreover, in this case caused considerable rectal irritation and tenesmus, doubtless from direct pressure on the rectal wall. Similar cases have been described by Dr. Ernest Herman,¹ and by Dr. Grace Murray, of New York. In my case anterior fixation of the uterus was attended by the happiest results, and no recurrence of the old symptoms had taken place two years later.

Enterospasm.

In two cases the cause of the constipation appeared to be a local spasm of the colon which produced severe pain and symptoms of obstruction. In one case (Case VII) the patient had a chronically inflamed appendix, strictured at its base and with a distended extremity, which at the time of operation was found to contain a drachm of pus. The other case (Case XIV) was a very remarkable one. The patient was a lady who had been a more or less complete invalid for ten years. She was highly neurotic, and it was very difficult to tell how much of her trouble was genuine. She had been labelled as a hopeless neurotic

¹ *Practitioner*, 1910, lxxxiv, pp. 561-66.

by several people who had seen her. She had severe constipation, and frequently passed complete casts of the bowel in mucus. During many of the attacks the pain was so severe as to necessitate the use of morphia, and on several occasions she was thought to be suffering from acute intestinal obstruction. I operated upon her in 1908, and found some adhesions of the sigmoid and a prolapsed ovary which was removed. An appendicostomy opening was established to enable her to wash out the bowel. After this she was very much improved in health for about a year, when severe attacks of abdominal pain and obstruction recurred, and were so severe that I was asked to do something more. I again opened the abdomen and discovered that the gall-bladder was full of gall-stones (forty-four were removed in all). After this operation she became absolutely well, and now for about two years she has remained in excellent health. I think that the severe attacks of pain accompanied by complete obstruction of the bowels which occurred in this case, and led to the supposition that the patient was suffering from some mechanical blockage, were due to an acute enterospasm of the colon set up by gall-stones probably passing down the ducts.

Case XXIX was a very curious one. The patient had quite the worst symptoms of auto-intoxication that I have ever seen, and, although he was perfectly clean, he smelt so badly that it was almost impossible to stay in the room. The wound absolutely refused to heal, and nothing that we were able to do would make the dilated bowel contract, or would insure an action of the bowels. There was no lesion discovered to account for the condition, and it appeared to be a case of progressive atony of the bowel occurring for a period of about two years, and ending fatally. The case was in many ways a mystery and, in my experience, unique.

I have ventured to bring forward this series of cases because the treatment of chronic bowel obstruction associated with auto-intoxication has lately been the subject of much discussion, and it has seemed to me that anything which will help to elucidate the real facts in these admittedly difficult cases and to discover the pathological causes which underlie the condition cannot fail to be of value at the present time.

I cannot agree with Mr. Arbuthnot Lane in considering that all these cases owe their causation to a common factor, or that they possess a common pathology. It seems to me that there are a great number of different causes of this condition, and I have attempted, with the aid of the cases at my disposal, to bring forward a number of

instances in which the causes and pathology have been ascertained beyond reasonable doubt.

Moreover, while I cannot but admire the brilliant operative results that Mr. Lane has achieved in so formidable an operation as excision of the entire colon in patients who are necessarily in a very bad state of health, I cannot agree with him in believing that so serious an operation is either necessary or advisable. I think better results can be obtained at less risk by discovering, if possible, the cause of the condition and remedying it directly, where possible; and where this is not possible, I think appendicostomy, which admittedly should be an operation almost without any mortality, will give results which can compare very favourably with excision of the colon.

LIST OF CASES.

Case I.—A lady, aged 48, was sent to me with constipation of many years' standing, which was much worse for one year. There was occasional vomiting and chronic abdominal pain. She was a neurasthenic. She had passed membrane, had frequently lost weight, and was a complete invalid. She had had several slight attacks of appendicitis. Operation: Appendix removed, which was very long and kinked. I found an extreme degree of visceroptosis. The condition of the patient was not improved.

Case II.—A lady, aged 26, was sent to me with a history of increasing constipation. She had had severe abdominal pain for which morphia had to be given, and bleeding from the bowel. There was a seven years' history; the patient was much worse for two years, and had become a complete invalid. Right-sided colotomy had been performed eighteen months previously. She was no better, and only weighed 6 st. 3 lb. A sigmoidoscopic examination revealed a stricture due to pericolicitis in the sigmoid flexure. Operation: Hyperplastic tubercular stricture was removed from the middle of the sigmoid. Resection and end-to-end anastomosis performed. There was a complete recovery. The colotomy was closed a year later. The patient is now quite well and weighs 11 st.

Case III.—A lady, aged 40, consulted me with a history of alternating diarrhœa and constipation for many years. Operation: I found a kink of the sigmoid flexure due to a long, loose loop falling down behind and to one side of the rectum, which itself had an unduly long mesentery. The meso-rectum was shortened by stitching. There was considerable improvement for a time, but the symptoms partly returned later. [N.B.—Probably the stitches were not holding.]

Case IV.—A gentleman, aged 45, complained of very severe attacks of constipation, accompanied by abdominal pain. He frequently passed mucous

casts, suffered much from indigestion, and his bowels only acted as the result of repeated enemata. He was a stout, well-nourished man. Adhesions on the right side were diagnosed. Operation: A complicated adhesion of the great omentum to the right loin, which was kinking the ascending colon, was discovered and remedied. The patient got quite well, and there has been no trouble with the bowels since, nor any pain. This is a year and a half after the operation.

Case V.—A gentleman, aged 38, of very nervous temperament, had been subject ever since he was aged 20 to severe attacks of abdominal pain, accompanied by constipation. These completely incapacitated him. He never felt well. He had tried innumerable treatments. Adhesions of the sigmoid flexure were diagnosed from sigmoidoscopic examination. Operation: A long band of adhesions was found passing from the lower edge of the stomach to the left iliac fossa, and others between the iliac fossa and the centre of the sigmoid flexure. These were divided. The patient got well and put on 2 st. in weight. Excellent result.

Case VI.—A lady, aged 50, complained of intractable constipation with frequent faecal impaction, only relieved with difficulty. Sigmoidoscopy revealed kinking of the sigmoid. She had been operated on some years previously for ovarian cyst. Operation: Extensive adhesions were found to the abdominal wall and between the sigmoid flexure and the left iliac fossa. Her doctor writes, eighteen months later, to say that she is in good health and much benefited by the operation.

Case VII.—A gentleman, aged 50, had a history of increasing constipation for nearly a year. A tumour in the sigmoid flexure was felt, which was thought to be a malignant growth. Operation: A large stercolith, largely composed of hair, was discovered in the sigmoid, and removed through an incision which was subsequently closed. Complete recovery.

Case VIII.—A gentleman, aged 50, who for some time had been steadily losing weight, was sent to me. He was much wasted, had an earthy-coloured skin, and suffered from chronic constipation. He never felt well and was prematurely old. He was so ill that he looked unlikely to live more than a few months. Operation: Appendicostomy was performed. He got completely well, and eighteen months after the operation was in better health and weighed more than ever before in his life.

Case IX.—A lady, aged 42, was suffering from intractable constipation. She had an earthy-coloured skin and was very thin and wasted. She was a chronic invalid and threatened to commit suicide. Her bowels were never open except after repeated large enemata, and there was severe abdominal pain. Operation: Appendicostomy was performed. There was some improvement, but the patient was far from being cured. Probably some obstruction was overlooked in this case, and a further operation would be advisable.

Case X.—A lady, aged 52, for seven years had had attacks of abdominal pain, accompanied by severe constipation and large quantities of mucus in the

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stools. The attacks had been getting worse, and she seldom felt well. Operation: Chronic appendicitis with empyema of appendix found. The appendix was removed, and the patient was cured.

Case XI.—A lady, aged 31, had suffered from severe obstructive constipation nearly all her life. The bowels never acted normally, and defaecation was usually accompanied by pain. Operation: A tough band of adhesions was found between the middle of the sigmoid and the left iliac fossa. The patient was completely relieved by the operation and was delighted with the result one and a half years later.

Case XII.—A lady, aged 30, had suffered from very severe constipation for nearly two years. There was blood at times in the stools, and severe abdominal pain. She was markedly neurotic. Operation: Appendicostomy. A considerable degree of visceroptosis was found. The patient was relieved, but the case is too recent to know the result.

Case XIII.—A man, aged 29, had suffered from severe constipation for five years, accompanied by severe pain in the back and sacrum. Medicine gave no relief. A kink of the pelvic colon was diagnosed. Operation: I found the pelvic colon had an 8 in. mesentery, and had been kinked on itself. The mesentery was shortened by stitching. There was considerable improvement, but the patient was not cured.

Case XIV.—A lady, aged 29, had had very severe attacks of constipation and abdominal pain for ten years. She was almost a complete invalid. Only large enemata would relieve the bowels. She nearly had colotomy performed on several occasions for supposed obstruction. Appendicostomy gave some relief, but the patient still had attacks. A second laparotomy revealed gall-stones, which were removed. There was complete and absolute recovery. Probably irritation from the gall-stones had caused spasm of the colon.

Case XV.—A gentleman, aged 22, had suffered from very severe constipation all his life. The constipation culminated every few months in an attack of obstruction which, on several occasions, threatened his life; and relief could only be obtained by manual removal of faecal material under chloroform. Sigmoidoscopic examination revealed well-marked congenital dilatation of the pelvic colon, the diameter of the dilated colon being 9 in. Operation: Appendicostomy was performed to enable the dilated colon to be kept washed out. This afforded considerable relief, and the patient has since had no serious attack—that is for three years.

Case XVI.—A lady, aged 32, had suffered from severe constipation for twelve years. She became very much worse, and no drugs would give relief. There was abdominal pain, loss of weight, mucous casts in the stools, and severe visceroptosis. Operation: Appendicostomy. This gave great relief, and the patient put on weight and got practically well. She still remained rather neurotic about herself. All signs of auto-intoxication, previously present, disappeared. Three years afterwards she still had to use the opening, but was in good health and of normal weight.

Case XVII.—A woman, aged 45, came to me with a twelve years' history of abdominal pain and constipation. She frequently had severe attacks, with vomiting at times. She had had every sort of treatment. Operation: Extensive adhesions were found beneath the stomach, transverse colon and anterior abdominal wall (presumably the result of a perforated gastric ulcer, of which there was a doubtful history). The adhesions could not be separated. Appendicostomy was performed. The patient improved; the attacks stopped and she was much better, but not quite well.

Case XVIII.—A lady, aged 31, was sent to me from Australia, with a history that she had been an invalid for ten years. There was severe abdominal pain, and tenesmus, and constipation alternating with occasional diarrhœa. Diagnosis: Retroflexed uterus and adhesions of the pelvic colon. Operation: I found the centre of the pelvic colon kinked by adhesions to the iliac fossa. These were divided and the uterus was fixed in the normal position. The patient got perfectly well, and all the old symptoms entirely disappeared. She wrote later from Australia to say she was quite well.

Case XIX.—A gentleman, aged 25, came to me with a three years' history of constipation which could not be relieved by aperients. There was also abdominal pain. Operation: The centre of the sigmoid flexure was found sharply kinked by a band of adhesions to the left iliac fossa. The adhesions were divided. The patient got quite well, and the bowels acted easily. Two years later he was still well.

Case XX.—A lady, aged 62, had had increasing constipation for seven years. It was not relieved by aperients, and finally culminated in obstruction, for which colotomy had to be performed. This revealed a large tumour due to pericolicitis in the sigmoid. Four years later the patient was still in good health, but the removal of the tumour was hardly possible.

Case XXI.—A servant girl, aged 19, had suffered from severe constipation since childhood. She had been very bad for the last three years, and no aperient would produce any action of the bowels. Enemata often failed. There was marked auto-intoxication. Operation: Appendicostomy was performed. The patient became better. The auto-intoxication was quite got rid of, and as long as the opening was used the bowels acted regularly, but she could not do without daily wash-outs. There was no improvement in this respect three years later.

Case XXII.—A lady, aged 51, had for a year experienced severe and increasing difficulty in getting the bowels to act. She had occasional attacks of partial obstruction. The patient was very stout. A tumour was found in the abdomen. Operation: A large papillomatous ovarian cyst was discovered and removed. The patient was quite well a year later.

Case XXIII.—A gentleman, aged 53, had suffered from severe and increasing constipation for two and a half years, gradually getting much worse. There was pain in the left side of the abdomen and the groin. Aperients only acted uncertainly, and often not at all. Sigmoidoscopy was performed, and a

diagnosis of pericolicitis with stricture of the sigmoid was made and confirmed by X-rays. Operation (by another surgeon): A stricture, nearly 6 in. long, was found, caused by pericolicitis and diverticulæ in the middle of the sigmoid. Ileo-sigmoidostomy was performed. The patient recovered.

Case XXIV.—A gentleman, aged 46, had suffered from very severe constipation, which had been getting worse for some years. There was also pain in the left side. The sigmoidoscope revealed a pericolicitis stricture in the sigmoid. A mass was felt *per abdomen*. An operation was advised, but the patient put it off.

Case XXV.—A gentleman, aged 63, had had severe constipation for some time. This terminated in an attack of acute obstruction which was relieved with difficulty after repeated enemata. There was a tumour in the left side of the abdomen. Operation: Pericolicitis of sigmoid found. The stricture was resected, and the patient recovered.

Case XXVI.—A child, aged 7, had suffered from severe constipation for two years with occasional attacks of partial acute obstruction. The abdomen was of a great size. The child was wasting. There was a tumour in the right iliac fossa. The case was diagnosed as tuberculous peritonitis. Operation: Anastomosis was done between the transverse colon and the ileum. The patient recovered.

Case XXVII.—A man, aged 42, came to the hospital complaining of severe and increasing constipation, and severe abdominal pain located to the left of the umbilicus. There was no blood and the stools were normal. Operation: A large pericolicitis stricture was discovered in the sigmoid, adherent to everything, including two loops of small bowel. It was resected with difficulty, and a temporary colotomy performed. The patient completely recovered, but up to the present time (a year after the operation) he has refused to have the colotomy closed.

Case XXVIII.—A lady, aged 35, had suffered from severe constipation, abdominal pain, loss of weight, and constant headaches. There was a history of increasing trouble for two years. The pain was chiefly over the appendix region. Operation: An adherent appendix was removed. A very severe degree of visceroptosis was found. The transverse colon and lower part of the stomach were pelvic organs. The patient was much improved in health nine months later.

Case XXIX.—A man, aged 47, had been very seriously ill for two years with constipation and occasional attacks of diarrhœa. He had lost flesh to such an extent that he was a mere skeleton. His skin was of a dark grey colour, and had a most unpleasant smell which nothing would remove. The subcutaneous fat had entirely disappeared and there was considerable cutaneous pigmentation. The abdomen was greatly distended. There was no blood but some mucus in the stools, and the urine contained indican. He had a sub-normal temperature and a slow pulse. Operation: The whole of his intestines was much dilated and extremely thin, but no other lesion was found. Appendi-

costomy was performed in the hope of clearing the toxins from the colon. The wound refused to heal at all, and in spite of treatment the dilatation of the bowel persisted. The bowels at last refused to act, and although the small bowel was opened, he died, apparently from complete inactivity of the intestines, and toxæmia.

Case XXX.—A lady, aged 53, had for six months been suffering from severe and increasing constipation. The bowels only acted with difficulty, and aperients had constantly to be taken. There had been some blood in the stools, and a stricture—possibly malignant—was suspected. Operation: Laparotomy. No tumour or stricture was found, but there was an area in the sigmoid where the bowel was thick and apparently ulcerated for some inches. There was also an old chronically inflamed appendix. The appendix was removed and the abdomen closed. The patient recovered.

DISCUSSION.

The PRESIDENT (Mr. Clinton T. Dent), in thanking Mr. Mummery for his paper, said he would be glad to hear whether any member would be prepared to uphold the treatment of ileo-colostomy or similar proceedings for such cases as Mr. Mummery had brought forward.

Dr. HALE WHITE remarked that the part of the paper which afforded him most interest was that concerned with the formation of adhesions. Doubtless adhesions often led to constipation, but he thought there was often something more than mere adhesions. All must know of post-mortems on cases of tuberculous peritonitis in which the whole 30 or 40 ft. of bowel was matted together, and it would take hours to dissect it out. The marvel was in such cases that any intestinal contents found their way along at all. Yet in other cases quite a small adhesion obstructed the bowel. He congratulated the author on the advice given for overcoming the adhesions. He had had many such cases operated upon, but many surgeons were averse to operation because of the danger of such adhesions re-forming. But he could relate a remarkable case of an enormous mass of adhesions in connexion with the appendix. This mass caused constipation and pain lasting twenty years. It took two operations of two hours each to free them. But since they had been freed ten years ago the patient had been absolutely well in all respects. There was need for some guide as to why in some cases adhesions were so severe, and in others they did not occur. If they were present he agreed that they should be freed in the way Mr. Mummery suggested. With regard to the atonic cases, he agreed as to their unsuitability as a rule for large operations. Most of these patients were neurotic women, and some of them welcomed operation, and they might be operated upon until they were in a terrible state. He could recall one with two enormous scars in her abdomen where big operations had been done for atonic constipation, but she was not a bit better, and was a hopelessly bedridden

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woman. The operation in this case was short-circuiting from the ileum to the sigmoid. Perhaps it was that only the failures after operation came to the physician. His own feeling was that he had never seen atonic constipation so severe as to warrant surgical interference. If the doctor in charge would persevere with such treatment as exercises, abdominal massage, electricity, supports, stays, &c., and dispense with the pernicious use of aperients, he would often find the patient would get well and remain well. He could mention a case of a doctor who came to see him because he was so ill from constipation that he had determined to sell his practice. That was nine years ago; but he had been completely cured without operation.

MR. GORDON WATSON desired to congratulate Mr. Mummery on his paper, which had been brought forward at a very opportune time. The importance of Mr. Mummery's contribution, giving details of thirty patients suffering from marked constipation on which he had operated, lay in the fact that he had demonstrated in practically every case that there was a definite lesion which could be dealt with, and which he had dealt with in most of the cases with success. He hoped other surgeons would be able and willing to produce similar series of cases. He was particularly glad to hear the author point out that the detection of kinks by skiagram did not necessarily mean that they were pathological. Dr. Hale White had referred to the question of adhesions, and his own view was that sepsis was a very important element in the production of adhesions. When an operation was quite aseptic he did not believe that adhesions formed. With regard to Dr. Hale White's remarks on atonic dilatation of the colon, he certainly knew of one which had not responded to the various forms of treatment referred to. The dilatation had been demonstrated by giving a bismuth meal. The size of the colon was very great. The patient had been suffering from it for about six years, and had been carrying out various forms of treatment during that time. It seemed to be a case which did not respond to treatment, either medical or surgical.

MR. HAROLD CHAPPLE said he had been intensely interested in the subject of Mr. Mummery's excellent paper for some time. While he was in complete agreement with him as to the importance of the rôle played by auto-intoxication from the bowel, he could not agree as to the causes of the intestinal delay. He had himself seen quite a number of ileal kinks, and in his opinion there was no room for doubt as to their existence. It was scarcely possible to deal with such a large subject in a few minutes, but he would like to state that as a gynaecologist he had had the chance of dissecting a number of fetuses, and he did not find ileal kinks in them. He had also examined many women in the post-mortem room before any of the abdominal viscera had been removed, largely with the idea of becoming more fully acquainted with the pelvic viscera, and had found a variety of adhesions present in the region of the ileum. In actual practice he had seen their presence diagnosed beforehand; he had seen the bismuth meals obstructed at the end of the ileal portion of the gut, and when the abdomen was opened the kink was

found and undone. With regard to the treatment of this condition, if the mere undoing of the kink would only turn out to be sufficient it would be excellent, as no one wanted to remove colons unnecessarily, or to perform ileo-colostomy. But, unfortunately, experience showed it was not so, owing to the subsequent re-formation of the bands. The condition was frequently diagnosed as chronic appendicitis, and he had seen at least forty cases in which the appendix had been removed without producing any benefit. In these cases the ileum had been found to be obstructed in different degrees. He did not know whether surgeons would agree as to the causation of these adhesions, but as to their existence he thought there could be no doubt. He was much interested in the case spoken of in which the uterus was retroverted and rammed back on to the rectum. That was, in his opinion, a secondary condition. Intestinal delay was associated with auto-intoxication, and the products absorbed produced a loss of fat and tone in the uterine supports, with degenerative changes in the uterus itself, so that it became retroverted and its blood supply interfered with. The condition was treated frequently with a Hodge pessary, and the uterus was tilted forward, or it was sewn up to the abdominal wall, with a good result. This treatment did not, however, deal with a primary cause. In the treatment of intestinal stasis the one difficulty which had not been overcome was the occasional formation of post-operative adhesions. They were not, however, peculiar to this type of operation, as they occurred occasionally in all varieties of abdominal surgery, and all efforts at their prevention had, so far as he knew, proved futile. Their causation was quite obscure.

Mr. H. W. CARSON desired to raise one point. He understood the author did not deny the existence of the adhesions; indeed, to do so at the present day would be futile, because all surgeons must have seen them, and the more cases of chronic constipation were operated upon the more adhesions would be seen. In a number of cases of chronic constipation the main symptom was pain and tenderness, with its maximum at or near McBurney's point. It had been too much the habit to diagnose such cases as appendicitis, and the surgeon had been content when operating with removal of the appendix through a small incision. But during the last year or eighteen months he had been much struck with the fact that a larger incision, exposing the caecal region and the caput caeci, would bring to light a curious form of adhesion known by Americans as membranous pericolicitis. He had operated upon several such cases, and found it a very definite condition. On division of the kink the intestine at once unrolled itself, and the obstruction was over for the time. His experience had been much more in connexion with sheaths of membrane lying over the ascending colon than in actual ileal kinks; but he had seen the two conditions occurring together. He pleaded for a wider exposure of the abdominal viscera in cases of localized pain in the appendix region where the patient also had constipation.

Mr. MUMMERY, in reply, said it was true that in cases of tuberculous peritonitis one found children with the whole intestine matted together,

and that it was wonderful how anything passed through. It was well known, however, that the type of adhesion most liable to cause obstruction was a single localized band, which produced constriction by kinking. Where there was general matting there was not the same tendency to a localized obstruction. In answer to Mr. Chapple, he thought the whole subject required attention for some years to come, because it was most important to clear it up, and to find out what was the exact pathology of cases of chronic constipation. If every one who operated on these cases would publish their reports in detail, there would be a definite basis to go upon. The difficulty was that in many cases details were not published. His point about kinks was to advise caution about assuming that all kinks were pathological. He was quite familiar with the so-called membranous peritonitis, and he had met with cases in which a thin transparent membrane covered over several portions of the bowel, but he did not regard this condition as necessarily pathological, in the sense of producing difficulty of passage of the colon contents. One must accept with great caution the evidence derived from the dissection of fetuses in relation to the arrangement of the peritoneum. The cæcal angle was the part of the colon most liable to be abnormal, and there was extraordinary diversity in the arrangement of the peritoneum at that spot. That made one cautious about generalizing from post-mortem findings. It was difficult to know how much of the kinking was pathological in the production of obstruction, and how much was not. He believed the case in which the uterus was retroflexed was an exceptional one, and he did not think the retroflexion was the cause of all the symptoms. At any rate, after fixation of the uterus, the patient, who had been bedridden for twelve years, got well, and has remained so for several years.

A Case of Thrombosis of the Veins of the Colon causing Obstruction.

By H. W. CARSON, F.R.C.S.

THE patient was aged 73, very well preserved, and with a good previous history. He stated that his bowels had been irregular for the previous six months, with alternate diarrhoea and constipation; once he passed a little blood. He has of late had vague abdominal pains, as he says, "due to wind," and a fixed pain in the left iliac fossa. There has been no loss of flesh. One month ago he had an attack of partial obstruction.

November 16, 1910: In the morning abdominal pain, with vomiting and some distension. Relieved by enema.

November 17, 1910: Seen in consultation with Dr. Power, of Stamford Hill. Tongue clean, but dry; pulse 108. Is in some pain, generalized in the abdomen, and there is marked tenderness and some resistance in the left iliac fossa. The cæcum is a little distended. On rectal examination there is tenderness high up to the left, and there is blood on the examining finger.

Operation (November 18, 1910): Abdomen opened through left linea semilunaris. Rectum and sigmoid flexure are normal, but the colon from the hepatic flexure to the middle of the descending colon felt thick and boggy. There were recent adhesions at the splenic flexure, and two yellow spots like commencing perforations in the descending colon. The serous coat looked normal, except at these two spots. The affected part of the colon was resected, and an artificial anus left, the hepatic flexure coming easily across to the opening on the left side of the abdomen.

The patient made a good recovery, except that he was somewhat bothered by prostatic trouble, and left the nursing home on December 16.

Pathological Report.—"The colon presents at one extremity an area of ulceration on the inner surface. The muscle here is practically bare; for the rest of its extent the mucous membrane is raised in bosses, or tuberos-looking masses, with deep sulci dividing them from each other. These tuberos swellings have a dark purplish-red line, and they are faceted one against the other by mutual pressure, but their free surface is convex. One section has been taken from the ulcerated end, and another from the other. Histologically, the entire bowel wall is seen to be extremely œdematous. The peritoneum is fairly normal, but between it and the longitudinal muscle layer there are areas of fibrinous infiltration. The outer muscle coat is fairly well preserved. The middle coat is practically indistinguishable as such, its place being taken by a fibrinous exudation and tissue breaking down. The vessels here are in part empty, in part thrombosed. The mucous coat is very necrotic, the Lieberkühn's follicles are shrunken, and have largely lost their epithelium, and it is overlaid by a zone of fibrinous exudation. The submucosa is extensively infiltrated with inflammatory round cells. In places the true mucosa has disappeared, its place being taken by œdematous granulation tissue. There is no evidence of new growth. The condition appears to be one of acute phlegmonous colitis of diffuse type occurring in connexion with actual ulceration of a portion of the intestinal tract."—CUTHBERT LOCKYER.

A section through the ulcerated portion stained by Gram's method showed the surface of the ulcer and the underlying necrotic tissue crowded with slender Gram-positive bacilli and diplococci resembling the pneumococcus. A very few of these latter were also found deeper in the tissues.

Exhibits: The colon, a coloured drawing of the same, and microscopical sections.

DISCUSSION.

Mr. LOCKHART MUMMERY said he considered that the case was one of mesenteric thrombosis. The only comparable condition he had seen was one the specimen of which was sent him from Leeds, and a drawing of which he had used in his Jacksonian Essay. In that, however, there was not the same amount of œdema of the mucous membrane, but there was the sharp line at either end of the region; it involved practically the same portion of bowel, was in a patient of the same age, and the symptoms were similar.

Dr. HALE WHITE said that the sharp demarcation showed that the view taken was the most likely. The extraordinary point was that the thrombosis did not spread farther back into the other veins, or implicate a larger piece of gut. Sir William Gull recorded such a condition. It was difficult to know whether the block was in the artery or in the vein, unless one dissected it out.

A Case of Right Duodenal Hernia.

By H. W. CARSON, F.R.C.S.

THE patient was a man, aged 29. He was one of a family of twelve, eight of whom had died, the last one of a tuberculous throat disease. He was admitted to hospital on November 11, 1906. In 1902 he had had pain in the epigastrium, which lasted for a fortnight and passed off completely. This attack had no relation to the taking of food and there was no vomiting. In February, 1906, having been in perfect health in the meanwhile, he had a similar attack, and at the end of June, 1906, a similar attack, which has not altogether cleared up. He says he is troubled with "wind," which comes up to a painful spot in the epigastrium and then suddenly passes away. The painful spot is slightly above and to right of umbilicus. He has vomited on several occasions, but managed to take food well. Since this attack his bowels have been loose about twice a week, with constipation at other times. He has not lost flesh. For the last fortnight vomiting (dark green material) has occurred every day or two.

Condition on admission: Pale and very thin. Lungs, heart, and urine normal. Abdomen emaciated, with lax walls; free from tenderness, except at a spot just to right of umbilicus, where there is also some resistance. Bowels not open.

November 12, 1906: Distinct lump in epigastrium, a little to right of umbilicus; dull to percussion. Constant vomiting of bright green material.

November 13, 1906: Peristalsis from left to right in lower epigastrium. Lump as before. Bowels not open.

November 15, 1906: Inflation shows stomach dilated to below umbilicus.

November 17, 1906: Constant vomiting. Losing strength. The epigastrium is occupied by a smooth distension, but below the umbilicus the abdomen is concave. Bowels have not been open since admission, but flatus has followed an enema.

Operation: Median epigastric incision. The stomach and first two parts of the duodenum are distended, the rest of the duodenum and small intestine is invisible. Lying to right of the pylorus are two portions of intestine apparently linked together—one duodenum, the other the ascending colon. The veins of the descending colon and sigmoid are enormously dilated. The ascending colon and cæcum have long mesenteries; they are collapsed, but the ascending colon contains some hard faecal material. The small intestine was withdrawn in a collapsed condition from a sac situated behind the peritoneum in front of the right kidney, and was found to have a double axial twist from left to right, completely obstructing the whole of the intestines at the neck of the sac. When the twist was released the two portions of intestine previously mentioned as linked together were freed also. It was now seen that the ascending portion of the duodenum and the duodeno-jejunal junction had a long mesentery and were not in any way fixed to the posterior wall. The neck of the sac was large, the anterior margin containing the superior mesenteric artery, the posterior containing the inferior mesenteric vein. No attempt was made to close the opening.

The patient made an uninterrupted recovery and was discharged on December 15, 1906.

This case is the eighteenth recorded, the last being reported to the Clinical Society in 1906 by the late Mr. Percy Paton.¹

¹ *Trans. Clin. Soc. Lond.*, 1906, xxxix, p. 139.

The site of origin of this hernia is still a matter of debate. Klob, who reported the first case of right duodenal hernia in 1861, suggested that they originate in the inferior duodenal fossa. Treves, Jonnesco and Treitz are of the same opinion. Moynihan maintains that left duodenal hernia arises in the paraduodenal fossa of Landzert, right duodenal hernia originating in the fossa of Waldeyer. Gruber, in 1862, maintained that right duodenal hernia was due to a right-sided position of the fossa duodeno-jejunalis of Treitz, the duodenum, instead of terminating on the left side of the spine, taking a shape like the letter **S** and terminating to the right of the lumbar vertebræ. Brösike maintained that for a right duodenal hernia to occur there must be a fusion of the first few inches of the jejunum with the posterior wall. The two last opinions are so absolutely opposed to one another that it is of interest to point out that in the present case the ascending part of the duodenum and the commencement of the jejunum had free mesenteries, and as in Gruber's case the duodeno-jejunal junction was to the right of the lumbar vertebræ. The point of outstanding interest in this case is the obstruction of the inferior mesenteric vein, which would suggest that it was in connexion with the neck of the sac. This vein forms the outer and upper edge of the neck of the *paraduodenal fossa*; it has been found, though not invariably, in the free outer edge of the *inferior duodenal fossa*, but it is some distance from the neck of the *fossa of Waldeyer*, and it is doubtful whether in the present case, as the intestines were collapsed, there would be sufficient traction at the neck of the sac to cause a drag on the vein. It is hardly possible that this case is an instance of a hernia into the *infraduodenal fossa* (of which only one case is reported by Moynihan), as the superior mesenteric artery has normally no relation to it. The axial rotation of the contents of the sac has been noted on several occasions.

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VOLUME THE FIFTH

COMPRISING THE REPORT OF THE PROCEEDINGS FOR THE
SESSION 1911-12

THERAPEUTICAL & PHARMACOLOGICAL SECTION



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Therapeutical and Pharmacological Section.

October 17, 1911.

Professor W. E. DIXON, F.R.S., President of the Section, in the Chair.

PRESIDENTIAL ADDRESS.

The Rationale of Acquired Tolerance to Drugs.

EXPERIMENTAL pharmacology has only comparatively recently developed from the stage of observation and description. Until about the middle of the nineteenth century the symptomatology of drugs was almost all we knew of their effects, and although this may be useful enough in its way, it affords no real insight into what we now call the pharmacological action of a drug. During this period of pharmacological evolution, but especially during the activity of Virchow, the thoughts of pathologists have been centred on the search for the seat of disease, and there can be little doubt that one effect of cellular pathology has shown itself in the treatment of patients by the change from the voluminous prescription to the simple one containing one or two drugs. But the most hopeful indication of the progress of medicine towards the ideal of Descartes is to be found in the advances made by experimental pharmacology in recent years, and it is difficult to doubt that the pharmacologist of the future will supply the physician with the means whereby he may influence in the desired way any tissue in the body. Not a few such specific drugs we are already acquainted with, but it is to a single small feature in their action that I propose to confine my remarks to-day. I refer to the phenomenon of immunity, or, more correctly speaking, tolerance.

The hypothesis of Ehrlich, the nomenclature associated with which has come to form a language of its own, to account for the action of

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toxins and drugs, is familiar to everyone. In the words of Behring: "The same substance which when incorporated in the cells of the living body is the pre-requisite and condition for an intoxication, becomes the means of cure when it exists in the circulating blood." Ehrlich supposes that food substances attach themselves directly to a receptor in the cells of the living body, and that these same receptors may also combine with toxins and cause disease. For it can hardly be supposed that the animal body is endowed with separate receptors especially designed to meet pathological emergencies.

The existence of receptors can be proved by experimental methods. This was first demonstrated by Wassermann, who showed that the cells of the central nervous system which were known to be affected by tetanus toxin anchored the toxin. But Ehrlich adopts the view that drugs also are attracted by and bound to the protoplasm molecule by atomic groupings. Ehrlich does not regard these as food receptors, and it is difficult to consider them from an evolutionary standpoint as being specially designed for the benefit of the pharmacologist and physician. It will be necessary, however, to refer to the subject later.

One of the simplest known ways in which the organism is able to protect itself against poisons is represented in the case of the aromatic series of drugs which I might briefly exemplify by carbolic acid, camphor, and salicylic acid. The first of these combines in the body with sulphates forming $C_6H_4OH.SO_2OH$; the second of these, camphor, with glycuronic acid; and the third, salicylic acid, combines with glycocoll, forming salicyluric acid; but the result of these combinations in each case is to form a relatively non-toxic substance. Salicyluric acid, for example, has little antiseptic action, and is without beneficial effect in acute rheumatism. The synthesis in this substance takes place largely in the kidney, but to some extent in other tissues, and there is evidence to show that it is brought about through ferment agency. Methyl-salicylate, on the contrary, is excreted, according to Baumann and Herter, as the ethereal sulphate, an innocuous substance like salicyluric acid.

The difference in toxicity of carbolic acid from its ethereal sulphate is also very decided, and it would naturally be suggested that the injection of sulphate should be the treatment to adopt in cases of carbolic acid poisoning. In practice, however, little benefit has followed injections of sulphate in acute poisoning, though this treatment has been more successful in some chronic cases. It is well to remember that carbolic acid and sodium sulphate have no chemical affinity for one

another *in vitro*. The combination with sulphate in the body is brought about only slowly, too slowly to make sulphates of much value as an antidote in acute poisonings; this fact also agrees with the view that the combination is the result of a ferment action.

Possibly chloral, though not belonging to the aromatic series, affords another example of natural protection; it combines in the body with glycuronic acid to form urochloralic acid. The synthesis of this instance does not occur in the kidney, but almost entirely in the liver, and again, the evidence points to its being brought about by the action of a ferment. Teleologically some such protective mechanism is a necessity in the case of the aromatic substances, since several of these bodies are formed in the alimentary canal during digestion; and as the result of putrefaction, and after absorption they might cause poisonous symptoms, unless they were neutralized.

It is not so much with these cases of natural tolerance that I wish to deal to-day, as the mechanism by which the body can increase its tolerance to a foreign substance. Perhaps alcohol, if we may regard this substance as a drug, though we cannot altogether regard it as a substance foreign to the body, affords the most familiar example. It is completely oxidized and destroyed in the body in physiological dosage, but the rate of oxidation appears to vary in different individuals, and so soon as the blood contains a certain percentage, somewhere about 0.1 or 0.2 per cent., symptoms associated with the central nervous system become manifest. Those, however, addicted to the use of strong beverages may take an amount of alcohol without apparent effect on the central nervous system which would profoundly influence the self-control of the average moderate person, and this is not because the alcohol has not been absorbed, but probably because the rate of oxidation is better able to keep pace with the rate of absorption. It is interesting here to note the explanation which has been generally accepted in the past, that "tolerance depends on a gradual habituation of the tissues to the poison," an explanation which to me explains nothing.

It is, however, more particularly in the case of alkaloids that an acquired tolerance can be obtained. There can be little doubt that morphine is broken up in the body possibly into oxy-di-morphine, a substance which possesses little or no morphine-like effect. After hypodermic injections of morphine into the dog, Faust has shown that 70 per cent. can be extracted from the fæces; habituation, however, leads to diminution in the amount excreted until a stage is reached when daily injections can be given without more than a trace of morphine being

excreted. Post-mortem chemical analyses of the tissues of such a dog showed the absence of the alkaloid. This certainly looks as if artificial tolerance were produced in this instance by the increased power of the tissues to destroy the alkaloid.

Heger and others showed many years ago that animal tissues possess the power to destroy certain alkaloids. If the tissue juice squeezed out from a frog's liver, and filtered so as to be entirely free from microscopical particles, be mixed with a little hyoseyamine and kept at 22° C. for two or three hours under suitable antiseptic conditions the alkaloid disappears; both chemical and physiological tests yield negative results. The same effect can be obtained in the rabbit, but it is less marked; the dog's liver, on the contrary, has little or no destructive power. Cloetta, following on these lines, has recently given an explanation of the natural tolerance of rabbits to atropine. These animals, after receiving an injection of atropine, normally eliminate 15 to 20 per cent. in the urine during a period of from two to three days. But if the animal has been receiving daily injections of atropine for some weeks it is found that after a single large injection no alkaloid is present in the urine after twenty-four hours, nor can it be detected in the tissues after death. This fact is partly due to increased power of destruction by the liver, and partly to increased rate of excretion. The natural immunity of the rabbit to atropine depends mainly on its power of destroying atropine, and the sensibility of the cat on the absence of such power; but in both animals, during artificial immunization, the atropine is excreted by the urine more rapidly.

Some five or six years ago Dr. Lee and I started some experiments on toleration to nicotine with a view to determine the character of the tolerance, and our experiments are now completed. An abstract of them was published some years ago in the *Proceedings* of this Society.¹

It is now clearly recognized that men can acquire some small degree of tolerance to tobacco smoking, and it is proved that the toxic effects of smoking are due to the nicotine, the other products being altogether insignificant in comparison with this substance. Nevertheless investigators differ as to whether a tolerance can be acquired by animals. Kobert, Esser and Edmonds find that some small degree of tolerance can be acquired. Gouget, Lesieur and Richon and Perrin say that tolerance is not obtained by repeated injections of nicotine. The literature seems to be consistent in the fact that small or moderate injections of nicotine administered occasionally always produce the usual

¹ *Proceedings*, 1908, i, pp. 37-8.

physiological effect, therefore several writers say tolerance cannot be obtained. In other words, no matter what previous injections the animal has had, if nicotine can reach the tissue upon which it acts it produces its normal effect. This leaves only two probable explanations of the tolerance in man. The first is that, in the tolerant man, nicotine is not absorbed. A great deal of clinical evidence is at hand to rebut this supposition, as it is well known that excessive smoking readily produces toxic effects—alimentary, cardiac and nervous—even in the most inveterate smokers. There is no jot of evidence in support of this speculation, indeed all the direct evidence is against it. The second explanation is that the nicotine is destroyed as an active substance, but that the rate at which destruction occurs is limited. If the destruction were carried out slowly by the tissues as the oxidation of alcohol and sugar is carried out, that would not necessarily prevent its exerting a physiological action, and if the rate of absorption exceeded that of destruction a nicotine action would certainly be obtained. Moreover, if the nicotine were introduced directly into the circulation, the destruction under these circumstances, that is within a few seconds, would be practically *nil*, and so the whole of the specific action of the nicotine would be obtained, no matter what the degree of tolerance might be. The conclusion to be derived from previous observers seems to be that repeated small injections of nicotine lead to little or no tolerance if the test of the tolerance is to be the visible effects of a large injection.

Animals certainly exhibit some tolerance after repeated injections of very large toxic doses of nicotine, using the same test as before as a sign of tolerance, as has been shown by Esser, Edmonds, and others. But the effect of these large toxic doses is to cause, after a preliminary stimulation, general depression of nerve-cells throughout the body, so that subsequent injections of nicotine lose some of their stimulant action. In any case it has not been shown that this so-called "tolerance," brought about in this way, is not simply the physiological action of the drug, and there is no reason to regard it as other than this until it is shown to be a true tolerance.

It is not, however, with these instances in which enormous doses of nicotine were administered that the tolerance to nicotine is of interest, but rather with the small doses of nicotine taken regularly. Edmonds has summed up these cases by saying that tolerance to nicotine or tobacco can be obtained in animals only with great difficulty. Two points, however, require consideration. First, is the test of tolerance valid? In Edmonds's experiments it was vomiting following

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on subcutaneous injection. Reasons have been given already to show that this might be so in certain forms of tolerance, but that if the tolerance were due to a gradual destruction of the alkaloid it is not valid, and secondly, if the nicotine is given by the mouth it must be so diluted as to exert no irritant action on the mucous membrane of the stomach, for the vomiting in the latter case would be reflex and would afford no evidence of the presence or absence of specific tolerance.

The present experiments were undertaken to test the validity of the hypothesis that nicotine tolerance is due to the destruction of the alkaloid by the tissues. I will not trouble you with the technical details of these experiments, which will be published elsewhere. Briefly, the experiments were as follows: Rabbits were injected every second or third day with small doses of nicotine, receiving ten to fifteen injections in all. They were then killed and the liver was completely broken up and extracted with water; a second liver from a normal rabbit from the same litter was treated in the same way, and to each liver emulsion, freed from all microscopical particles by filtration through a filter-cloth, a definite quantity of nicotine was added with a sufficiency of toluol to prevent putrefaction. The two emulsions were incubated at body temperature for a period of three hours, and the nicotine was then estimated in each. The amount of nicotine in each was found to have diminished, but that in the tolerant liver was diminished to a greater extent than in the other. In only two experiments out of seventeen was no difference detected between the two livers. In other words, the liver can destroy nicotine, but if the animal during life has been habituated to the alkaloid, then that liver could destroy more, weight for weight, than the normal liver. If the liver is first boiled then its power of destroying nicotine is completely lost.

Two possibilities now present themselves: either the nicotine combines with some constituent of the extract present in larger quantities in the tolerant animal, and which renders the alkaloid inactive, or the nicotine is destroyed, possibly by oxidation. If the first supposition were correct it would be legitimate to expect to obtain as great a destruction of the alkaloid by shaking up the liver extract with nicotine for a few minutes as for a few hours, provided, of course, no loss by evaporation occurred, but this is not what happens. The loss of activity proceeds only very slowly; this might be anticipated, for were the loss of activity produced suddenly it would be right to expect a large degree of tolerance in animals subjected to nicotine injections.

It does not then, *a priori*, seem likely that the cause of the loss of activity can be explained on the supposition of any sort of a chemical combination. The evidence, then, so far points to some form of destruction of the nicotine, possibly the process being in the nature of a ferment action. With a view to testing the validity of this hypothesis fresh livers from tolerant and normal animals were pounded in mortars with a liberal supply of toluol. The emulsion was spread on glass plates and rapidly dried in a current of air; it was then scraped off and pounded into a fine powder. These powders from normal and tolerant rabbits were able to destroy nicotine, but the destruction was greatest in the case of the tolerant animal. After keeping for ten days the two varieties of powder exerted an equal effect upon nicotine, which was very slight.

These additional facts point strongly to the conclusion that the destruction of nicotine is brought about by a ferment, as it is well known that ferments on keeping in the dried state may lose their activity. It is, indeed, difficult to conceive of any hypothesis to meet all these facts other than that suggested.

These experiments show that a certain degree of tolerance can be obtained to nicotine, and that this is brought about by the destruction of the alkaloid. The destruction goes on very slowly and it can never be accelerated to such a degree that an injection of a poisonous dose of nicotine into the circulation of an animal will lose any appreciable amount of its effect. If the nicotine reaches the circulation slowly and in minute quantities it may be dealt with by the tissues, and this is the condition which obtains during tobacco smoking. The condition is exactly analogous to that of the hardened drinker; so long as destruction of alcohol can keep pace with absorption intoxication can be avoided, for we know that for practical purposes no alcohol is excreted from the body as such. Although, then, there is strong evidence in support of the view that tolerance means increased rate of destruction, yet there is some evidence suggesting that the nicotine is taken up specifically by certain tissues. Heger and others have shown that when nicotine is injected into the circulation of animals it disappears quickly from the blood, and is taken up by the liver, from which it can be obtained again by distillation.

These two facts, then, that the nicotine is picked out from the circulation by the liver, and that it is this organ especially which brings about its destruction, are, we believe, the main factors concerned in tolerance to nicotine.

The explanation of acquired tolerance which has been offered for certain organic substances and alkaloids cannot apply to the acquired tolerance which can undoubtedly be induced to certain inorganic substances. It has been long known that a small degree of tolerance can be produced towards gastro-intestinal irritants. Thus a certain small degree of immunity can be acquired for such irritant emetics as copper sulphate and zinc sulphate, and for the vegetable purgatives. The tolerance towards arsenic affords another example. Brouardel and other observers have found no evidence that dogs can become accustomed to arsenic provided it is injected under the skin; sometimes, on the contrary, they became more susceptible. Cloetta found that if the arsenic were administered by the mouth the dogs did acquire some tolerance, and that by gradual habituation two, or even three, lethal doses might be administered by the mouth without very severe symptoms, and yet the dogs succumbed to the minimal lethal dose when this was placed under the skin. He explains this on the supposition that the drug is not all absorbed when taken by the mouth, but that much passes out with the fæces. In man there is also abundant evidence to show that certain individuals can acquire some degree of tolerance, though several experimentalists, working in laboratories, have tried and completely failed to induce such a condition. Recently, a prolonged attempt was made in our Cambridge Laboratory, but without success, for as soon as the drug was pushed nausea, conjunctivitis, and a papular eruption appeared, so that after some weeks of trial the attempt had to be abandoned. Tschudi says that the arsenic eaters of Styria begin with doses of 0.02 gm. to 0.03 gm. of arsenious acid and that they take this dose two or three times a week; he puts the maximum dose these people take at 0.42 gm., and states that, excepting on rare occasions, injurious effects are wanting. Hausmann considers it proved that arsenic eaters can take without ill-effect a dose of arsenic that to a normal man would be fatal. Clinical reports leave us no option but to believe that certain men may acquire a tolerance which cannot be explained altogether on the supposition of non-absorption, since in some instances relatively large quantities of arsenic have been extracted from their urine. May it not be that the immunity is caused by the combination of the arsenic with some organic substance, resulting in the formation of an indifferent body free from arsenical action, just as the cacodylates are free from arsenical action until they are broken up in the body? In support of this hypothesis it may be mentioned that the arsenic excreted in the urine appears to be in some organic form.

Tolerance to arsenic may be acquired by protozoa, such as the spirochaetes of relapsing fever and trypanosomes. It is well known that Ehrlich gradually produced atoxyl-fast strains of trypanosomes which when injected into mice, the animals with which he worked, produced a trypanosomiasis which atoxyl even in the largest possible doses failed to influence; nevertheless, in some strains the protoplasm of the parasites is hypersensitive to arsenical preparations. It becomes necessary, therefore, to explain how this resistance and hypersensitivity come to be associated, and if we can obtain a rational understanding of the state of affairs, it can hardly fail to throw light on the tolerance in the higher animals. The facts are, then, that these particular trypanosomes *in vivo* are uninfluenced by arsenical preparations, but *in vitro* they may be even less resistant than ordinary trypanosomes. The only interpretation of this fact which I can conceive is that this breed of hypersensitive trypanosome can pick up a shield from the organism on which they are parasitic as a means of protecting themselves from arsenic, and one such shield might well be a chemical substance of such a nature that a combination occurred between it and the arsenic whereby a non-ionizable arsenical compound was produced, in exactly the same way as salicylic acid is rendered non-poisonous by combining with glycocholl. Or we might imagine that this breed of trypanosomes contains a relatively large amount of a ferment facilitating the combination of an organic substance contained in the blood with arsenic. Ehrlich, of course, attempts to explain the phenomenon on the chemo-receptor hypothesis, by supposing that the arsenic combines directly with the protoplasm molecule by certain atomic groupings. Now, some of these resistant trypanosomes, as we have seen, are more sensitive to arsenic in the test-tube than ordinary trypanosomes, and to me it is no explanation to say that the affinity of the chemo-receptors has become adjusted in such manner to the counterbalancing affinity of the mouse organism, that in the mouse no more arsenic remains at the disposal of the trypanosomes. After all, these are but speculations, and the correct solution can be obtained only by experiment.

Laburnum Poisoning and Cytisine.

By P. P. LAIDLAW, B.C.

THE common laburnum tree, *Cytisus laburnum*, was shown by Gray, in 1862 [1], to contain an alkaloid which he named "cytisine." This alkaloid has been found in a number of other plants, and has since been investigated from a chemical point of view by Husemann and Marmé [2], Partheil [3], and others. Its physiological action has been examined and described by Gray, Husemann and Marmé, Cornevin [4], Prevost and Binet [5], and Radziwillowicz [6]. The poisonous effects of laburnum are usually attributed to the presence of cytisine in the plant. As Dr. Dale and I have recently been engaged in re-investigating the action of cytisine, and have been able to determine its pharmacological effects with greater accuracy and fuller detail than previous workers, I thought it might be interesting to analyse a number of poisoning cases in man, and show that such new facts as we have discovered confirm the view that the alkaloid is responsible for the poisonous properties of the plant.

A large number of cases of accidental poisoning are recorded. Radziwillowicz collected 181 cases in 1888, and since that date additional cases have been described. The great majority of these occur in children, and are for the most part mild; fatal cases are rare. Three are described in the *British Medical Journal* [7 and 8] and one in the *Lancet* [9]; Radziwillowicz records others. The milder cases [10] run a course somewhat as follows: A child swallows a few laburnum seeds under the impression that they are peas; or he eats the flowers, pods, or leaves, possibly in search for a new sensation in flavours. About an hour afterwards the child feels unwell, complains of being unable to walk, or seems weak and helpless. Some complain of headache, giddiness, and stomach-ache. Shortly after the onset of these symptoms he vomits and appears to be very ill. The skin of the face in particular is pale, cold, and moist, the pulse rapid and thin. The pupils may be contracted at first, but dilate in the later stages; they react to light in mild cases. Sickness continues, and purgation may occur.

The recorded cases among adults are not severe, and usually have their origin in the mistaken use of laburnum flowers to flavour dishes.

Their use for this purpose is due to the cook mistaking the flowers for those of *Robinia pseudacacia*. Vallette [11] records one instance of this accident. A household of four members, three females and one male, partook of some poisoned fritters. The three women suffered from mild laburnum poisoning, the man developed no symptoms. The earliest symptom in one of these cases was a sensation of numbness in the hands and inability to play the piano. She was assisted to bed, where the symptoms were very similar to those already described.

The symptoms in a severe case are well illustrated in the following abstract from the *Lancet* [12]:—

J. W., aged 6, ate a hearty tea at 6 p.m.; at 8 p.m. he swallowed some laburnum seeds, saying they were peas. At 9 p.m. he appeared to be very ill, and vomited. Seen shortly afterwards, he was very pale; skin cold and clammy to the touch; pupils contracted; drowsy at times, but could be roused readily. There was no pain. Pulse, 108; axilla temperature, 97.5° F.; respiration 22. At 10.15 p.m. the drowsiness was more marked; the pupils dilated; pulse 130 and very weak; respiration, 25; rectal temperature, 96° F. At 10.30 p.m. the patient could only be roused with difficulty. The skin was very cold and bathed in perspiration; the pupils were widely dilated and insensitive to light. Caffeine was administered hypodermically, and a hot bath ordered. A mixture of ammonia and ether was given by the mouth at short intervals. After the hot bath improvement was noticed, and the symptoms gradually subsided. At 2 a.m., the child was sleeping peacefully, and next day was comparatively well, though the pupils remained dilated for twenty-four hours longer.

In fatal cases the symptoms are similar; the drowsiness becomes more pronounced as intoxication progresses, and the patient ultimately becomes comatose, with widely dilated pupils, which are insensitive to light; the respiration becomes stertorous, and cyanosis of the lips develops; the pulse becomes very rapid and the blood-pressure low. Death is due to respiratory failure, with or without convulsions [13].

In a limited number of cases symptoms of acute enteritis appear to be superimposed on the usual series. A striking example of this type of case is recorded by Wheelhouse [14]:—

A child, aged 5 years and 7 months, had been unwell for two days before being seen, and admitted having swallowed some laburnum seeds. On the third day more seeds were eaten, and the usual symptoms of laburnum poisoning developed. Vomiting and diarrhoea were, however, marked symptoms and could not be controlled. The patient was drowsy, then restless and irritable by turns. The pressure of the bedclothes appeared to be irritating, and they were repeatedly thrown off. For three days these symptoms were

present, and very little fluid was retained, although the patient was very thirsty. Temporary improvement was noticed on the fourth day, and fluids were retained better, but the progress was not maintained, and death ensued on the sixth day.

It has been suggested that the symptoms of acute enteritis, which are sometimes seen in cases of laburnum poisoning, are due to some unknown, highly irritating substance in the plant. They do not appear regularly, however, and may be examples of idiosyncrasy in response to cytisine. As far as I am aware they have no parallel in animal experiments with the alkaloid.

Post mortem, no positive signs of laburnum poisoning can be discovered apart from the isolation of the alkaloid from the viscera [13], and as this is present in other plants the evidence is inconclusive. In a few cases the mucous membrane of the alimentary canal is injected.

The treatment of laburnum poisoning resolves itself into removal of the poison by emetics or stomach-tube and the treatment of symptoms as they arise. Radziwillowicz has shown that cytisine is readily excreted in the urine; diuretics, therefore, seem to be indicated. In a number of cases hot baths seem to have been beneficial.

The action of cytisine on intact animals reproduces with fair accuracy the symptoms of laburnum poisoning in man. The herbivora are less susceptible than the carnivora. The goat is very resistant: slugs are immune. Shortly after a hypodermic injection of cytisine has been given to a dog, symptoms of nausea (salivation and uneasiness) develop, and vomiting follows. The pupils dilate and the nictitating membrane prolapses. With large doses or with intravenous administration the respiration first becomes hurried and deep, and later becomes slow, and may ultimately cease.

The respiratory and emetic effects are central in origin and are due to a stimulating action on the respective centres. The respiratory centre is readily paralysed with large doses. Muscular tremors are perceptible and weakness of the limbs is obvious. Large doses in anaesthetized or pithed animals under artificial respiration cause a complete paralysis of the nerve-endings in voluntary muscle (curare effect); about 6 mg. are required to produce this effect in a fair-sized cat. The muscular weakness may be the expression of a mild stage in this process. The pupil dilates in the cat under the influence of cytisine, and the nictitating membrane at first is withdrawn and later prolapses. If repeated doses of cytisine are given to a pithed cat, it is observable that the effect on the eye becomes less and less, until further doses produce

no effect. When this stage is reached it is found that the superior cervical ganglion is paralysed and that electrical stimulation of the cervical sympathetic trunk is without action on the eye, but stimulation of the branches from the ganglion to the periphery still causes normal

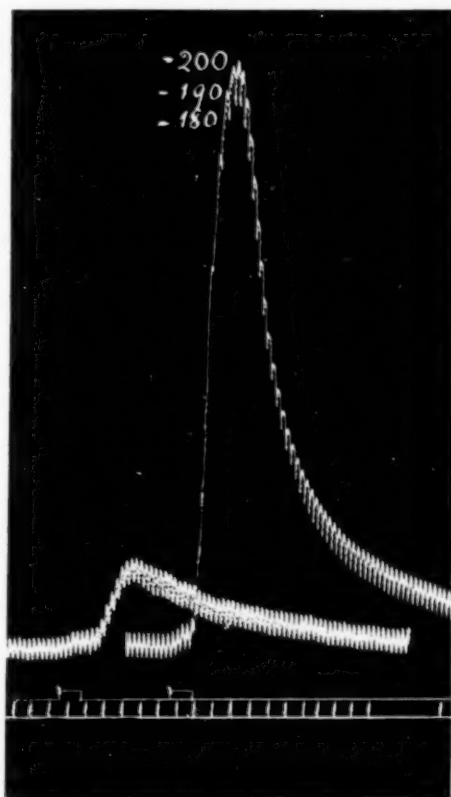


FIG. 1.

Cat, pithed. Artificial respiration; blood-pressure base line and signal; time in ten seconds. First curve, effect of 0.2 mgm. nicotine; second curve, effect of 0.2 mgm. cytisine.

responses. Once the ganglion system is paralysed with cytisine, nicotine is incapable of producing any effect. A flow of saliva is observable from the submaxillary gland of the dog and cat on administration of

cytisine. Large doses cause paralysis of the chorda tympani and render this ganglion system insensitive to nicotine.

On the blood-pressure cytisine exerts a series of effects, through its

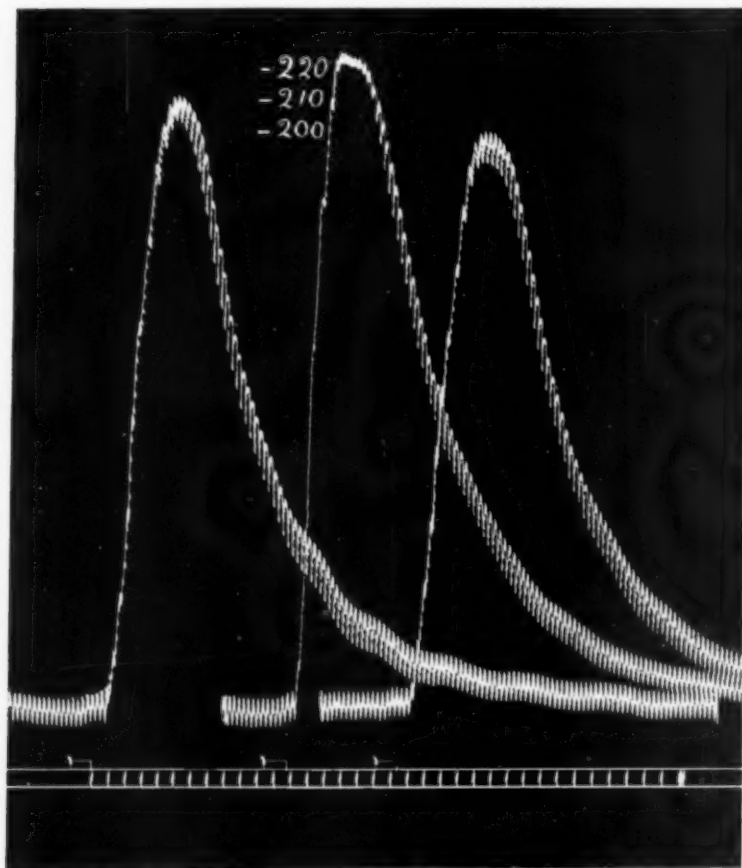


FIG. 2.

Cat, as in fig. 1. Effect of 1.5 mgm. nicotine; effect of 0.5 mgm. cytisine, and 1.5 mgm. nicotine.

stimulant action on ganglion cells. Thus the heart at first is slowed from a weak stimulant effect on the cardio-inhibitory apparatus, later it becomes very rapid, probably in part from stimulation of the stellate

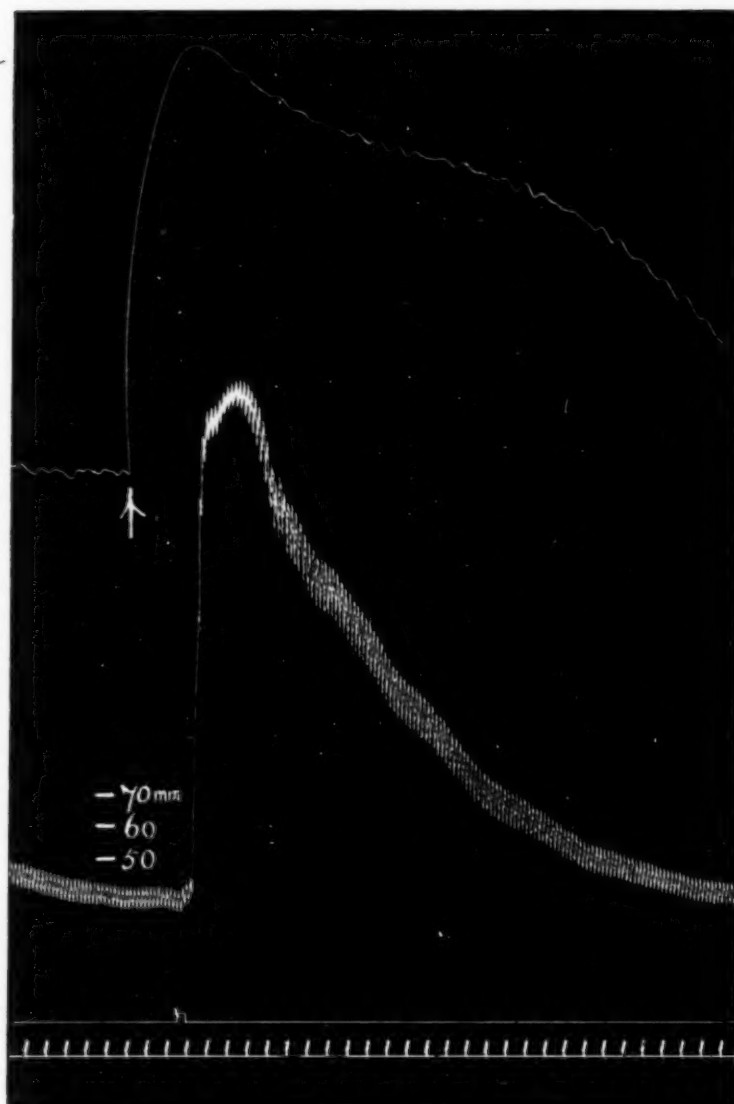


FIG. 3.

Cat, pithed. Artificial respiration, upper tracing bladder volume; blood-pressure base line and signal; time in ten seconds. Effect of 3 mgm. cytisine.

ganglion and partly from escape from vagus control. The arterioles are primarily constricted throughout the body, from stimulation of the sympathetic ganglia. These factors bring about a large rise of blood-pressure; with large doses the secondary paralytic action of the alkaloid becomes very marked, and the normal tone of the vessels cannot be maintained, and so the blood-pressure falls.

The intestinal movements in the cat are primarily inhibited, but subsequently become larger and more frequent. The bladder is thrown into a powerful and prolonged contraction, owing to the stimulating action of the alkaloid upon the sacral autonomic ganglia.

(At this point tracings illustrating the action of cytisine were shown by means of the epidiascope. Tracings showing the action of nicotine under similar conditions of experiment were also shown. Comparisons between these were made and the similarity in action emphasized.)

It will have been observed that these actions of cytisine which I have quoted are typical of the alkaloid nicotine. It is unnecessary to multiply examples from further experiments which were carried out in conjunction with Dr. Dale. I could quote many others which show the close similarity in action between nicotine and cytisine. Their resemblance in action is so close that by their action on animals alone it would be difficult to say whether a given solution was cytisine or nicotine. Edmunds [15] has shown that lobeline, the chief alkaloid of lobelia, has an action almost identical with that of nicotine. Apart, therefore, from isolation of the alkaloids themselves it would be difficult to determine whether one was dealing with nicotine, lobeline, or cytisine.

In conclusion, I should like to point out the similarity between cases of laburnum poisoning and nicotine poisoning. The man who can remember, as I do, his first overdose of nicotine through excessive smoking in the days of his youth has an excellent picture of laburnum poisoning. The restlessness, giddiness, tremors, muscular weakness, the nausea and salivation, the cold, clammy sweat, and vomiting, are all typical. In severe cases the widely dilated pupil, the drowsiness and coma, and the modes of death in both cases are very similar.

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DISCUSSION.

Professor CUSHNY, F.R.S., said he would like to hear whether there was a laburnum habit. The reason why Edmunds investigated the question of lobeline was that it had been discovered that lobelia was used by the North American Indians, particularly those of the northern part of the continent, instead of tobacco. In fact, lobelia was known as Indian tobacco, and there seemed every reason to suppose that this substance was used by Indians to a considerable extent. Langley showed, years ago, that pituri, from which another alkaloid, piturine, was derived, was used in Australia by the blacks, who were in the habit of chewing it, much in the same way as some people in this country use tobacco. So that those three alkaloids, which were practically identical in action, were used by various aboriginal races. Langley found that piturine acted in the same way as nicotine, and Edmunds could not distinguish the symptoms of lobelia poisoning from those produced from nicotine. There was found to be the same difficulty in obtaining satisfactory tolerance of lobeline as there was in the case of nicotine.

Dr. H. H. DALE desired in the first place to associate himself with the caution of his colleague as to attributing all the symptoms, which had been described as the result of laburnum poisoning, to the action of the alkaloid cytisine. He did not think there was any doubt that in the majority of cases the effect of laburnum corresponded closely to the effect of cytisine; but, as Dr. Laidlaw said, it looked as if, in a minority of cases, there were some other poison playing a part. The occurrence of enteritis, for example, was far more suggestive of the possible presence of some toxalbumin. One naturally suggested that, perhaps, because of the association with *Robinia pseudacacia*, the flowers of which had been confused with those of laburnum, with the result that some of the accidental cases of laburnum poisoning had arisen. In the second place, he had also had in mind the point which occurred to Professor Cushny. It was rather curious that mankind seemed to have an instinct for seeking out, and using for their enjoyment, alkaloids which had the particular action which had been described. It would be interesting to hear of the existence of a laburnum habit. As far as the records appeared to show, there was no indication of such a thing. The only other point which might be worth suggesting was the possibility of the therapeutic application of the

substance. It had been tried by two different people. Rose Bradford, many years ago, did some physiological experiments on the action of an alkaloid, which was described as ulexine, being isolated from the seeds of common gorse. This had since been identified with cytisine. Bradford, finding it caused diuresis when used experimentally in animals, tried it, he believed, in a few patients as a diuretic. What success it had in that direction did not appear to have been recorded. Radziwillowicz was struck, in his investigations, by its powerful effect in producing a rise of blood-pressure, and therefore tried it on certain patients who were suffering from migraine associated with low blood-pressure. He appeared to be under the impression that a favourable effect resulted. Now that the type of its physiological action seemed clearly established, the only reasonable suggestion of a therapeutic application was one similar to that for which lobelia had been used, and it would be interesting to know whether cigarettes made from laburnum leaves might have some value in cases of asthma, such as had been attributed to the use of lobelia.

Dr. W. MURRELL said he considered that the suggestion just made by Dr. Dale about using laburnum seeds in the treatment of asthma was a very good one. The idea occurred to him while the paper was being read.

Dr. T. R. ELLIOTT said an interesting inquiry would be to attempt to distinguish between the various nicotine-like bodies. The paper by the President analysed the power of the rabbit's liver, when the animal was made tolerant of the poison, to destroy nicotine itself to some extent; would it be capable of dealing in a similar way with the allied cytisine?

The PRESIDENT (Professor H. E. Dixon, F.R.S.) said the Section would wish to thank Mr. Laidlaw for his interesting paper. He (the President) desired to make only one remark, namely, that in acute cases of nicotine poisoning the symptoms came on with the fall of blood-pressure. He spoke of cigar smoking by young people. While the blood-pressure was going up, during say the first fifteen minutes, the smoker had a feeling of well-being; then the poisonous symptoms came on suddenly, the blood-pressure arrived at its maximum, and then dropped rapidly, and the smoker turned pale and showed the usual symptoms of collapse. In the case of three boys, he had found that the first symptom complained of was a rumbling in the abdomen, obviously associated with peristalsis, not vomiting; in one case there was definite diarrhoea. He suggested that that was possibly due to depression of the inhibitory sympathetic ganglia. By depressing those one cut off the inhibition, and the vagus was allowed to have all its own way for the time being, and there was increased peristalsis as a result. He mentioned this, because it was conceivable that those related alkaloids might have a different degree of effect. Cytisine alkaloid, for example, might have a more drastic effect on the alimentary canal than had nicotine, as the result of a more profound depression of ganglion cells, so the effect might conceivably be physiological, and not due to another substance.

Therapeutical and Pharmacological Section.

November 21, 1911.

Professor W. E. DIXON, F.R.S., President of the Section, in the Chair.

The Action of Potato-tyrosinase on Adrenalin.

By F. RANSOM, M.D.

THE red colour which develops in adrenalin solutions on standing is usually attributed to the formation of an oxidation product. It is accompanied by a diminution of activity, and Dixon found that the reduction of physiological activity was approximately proportional to the amount of coloration. The readiness with which oxidizing ferments act upon adrenalin has been frequently observed. On adding to a solution of adrenalin a tyrosinase which was contained in a fresh extract of *Russula delica*, Abderhalden and Guggenheim saw the formation of a red colouring matter. Neuberg found that the ink-bag of *Sepia officinalis* yields a ferment which converts adrenalin into a melanin, and that this black colouring matter is an oxidation product of adrenalin. Athanasiu and Langlois observed that adrenalin lost its pressor qualities when treated with ozonized air or with an oxydase obtained from crayfish blood. Batelli and Stern are of opinion that adrenalin is changed in the liver into ovyadrenalin. I have lately been making some investigations into the action upon adrenalin of a tyrosinase obtained from potatoes. A drop or two of a 5 per cent. solution of this tyrosinase added to 2 c.c. of adrenalin solution gives rise in two or three minutes to a pink colour which deepens rapidly to a port-wine red. Moreover, this reaction is very delicate; I find, for instance, that fifteen minutes after mixing the pink colour is quite evident in a solution containing less than 0.0004 per cent. of adrenalin: in 2 c.c. of solution this would equal 0.002 mgrm.

So delicate is the reaction that the presence of adrenalin in the suprarenals of a sheep may be readily demonstrated. A sheep's suprarenal is cut open lengthways, laid upon white filtering paper and a few drops of tyrosinase solution poured upon the cut surface. After a few minutes the medullary substance assumes a reddish tint, and if the fluid be allowed to run off the cut surface on to the paper the latter will be stained pink. The reaction is naturally not characteristic, both hydrochinon and phenol, especially the latter, give a very similar colour with potato-tyrosinase. The colour change does not take place quite so quickly with phenol as with adrenalin, nevertheless, one hour after mixing the pink colour is quite evident in a solution containing 0.0006 per cent. of phenol, so that the limit of dilution at which the coloration is observable does not differ very much from that found with adrenalin. The nature of the colouring substance thus formed is apparently not definitely known. Bertrand examined a number of bodies which give a similar reaction with a tyrosinase obtained from wheat-bran and came to the conclusion that the oxidation with tyrosinase is bound up with the C_6H_5OH group. In the case of adrenalin it is, perhaps, not unlikely that the red body may be orthochinon, but I have not gone into this point.

I find, further, that this change in adrenalin is accompanied not only by a loss of pressor activity but that also the power of inducing glycosuria is first reduced and then altogether destroyed. If the adrenalin solution is injected into the blood immediately after adding tyrosinase the rise in blood-pressure is practically the same as when adrenalin solution is injected alone. After the mixture has stood fifteen minutes the rise which now follows its injection is materially less, and after standing half an hour the mixture on injection causes no rise of blood-pressure at all. With reference to the production of glycosuria the same effects are observed; after the mixture has stood fifteen minutes some slight glycosuria follows its subcutaneous administration, but when it has stood half an hour no sugar appears in the urine after the injection.

The pressor action of tyramine (p.-hydroxyphenylethylamine) is affected in a similar manner by potato-tyrosinase. When the tyrosinase is added to a solution of tyramine the yellowish colour of the latter gradually changes to brown or black and there is a deposit of black material. The change of colour takes place more slowly than with adrenalin, but the resulting effect upon the pressor action is the same—after the mixture has stood a certain time the pressor action

is diminished and somewhat later disappears altogether; in fact, the changed tyramine solution produces a short but decided depression of blood-pressure. None of these effects are produced either so quickly or in the same degree when the tyrosinase solution is boiled before being used.

It seems probable that the red colouring matter formed by the action of tyrosinase on adrenalin is due to an alteration in the ring, but of course this does not exclude a simultaneous action on the side chain, and further investigations are needed to clear up this point. In any case, it is shown that by means of tyrosinase adrenalin can be deprived of the power of producing glycosuria and of its pressor action.

Glycosuria, however, does not always follow the administration of adrenalin. Underhill found quite lately that in endeavouring to reproduce Ritzmann's experiments he did not get glycosuria after intravenous injection of adrenalin unless the rabbits were under the influence of urethane. Pollak has shown that after repeated subcutaneous injections of adrenalin a condition of apparent immunity may be produced in which no sugar appears in the urine although considerable hyperglycæmia exists, and he concludes that the non-appearance of glycosuria is due to an increased resistance to the passage of sugar out of the kidney. Zülzer, Frugoni and Glaezner and Pick found that adrenalin glycosuria may be prevented by the administration of pancreatic juice. v. Fürth and Schwarz showed that in spite of hyperglycæmia the occurrence of glycosuria may be prevented by artificial irritation of the peritoneum. Schwarz found that adrenalin protects rabbits whose suprarenals have been removed against phlorizine diabetes to which they are otherwise very susceptible. To these facts I have now to add, as a result of my own experiments, that in rabbits the occurrence of glycosuria after subcutaneous administration of adrenalin may be prevented if immediately after the subcutaneous injection a dose of adrenalin is given intravenously and repeated two or three times at intervals of ten minutes. At first sight this appears to support Pollak's inference that there is increased resistance to the passage of sugar out of the kidney. I am at present, however, not prepared to offer an explanation or to agree with Pollak.

It appears from the foregoing that adrenalin may be so altered by oxidation as to lose both its pressor action and its power of inducing glycosuria. At what point or points in the adrenalin molecule the oxidation takes place is doubtful, but the very strong correspondence between the tyrosinase colour reaction with phenol and that with

adrenalin suggests that the hydroxyl groups in the ring are implicated. Further consideration will, however, lead us to think that this is not the only point where the oxydase effects a change. We have in adrenalin a body which when injected into an ear-vein of a rabbit, and so compelled before distribution to pass through the lungs, where we may assume oxidation readily occurs, does not cause glycosuria though retaining its pressor activity. That pressor properties may exist apart from or combined with sympathomimetic powers has been shown for numerous substances by Barger and Dale and others. It seems as if the oxidation of adrenalin in the body proceeds at two different points of the molecule and with different facility. The first and more easily accomplished oxidation takes place at a point which is concerned with the production of glycæmia; the pressor properties are not so easily oxidized into impotence. In correspondence with this, the dose of adrenalin which must be given to rabbits to induce glycosuria is very much larger than that which will cause a rise of blood-pressure. For example, 1 c.c. of a 1 : 100,000 solution of adrenalin injected into the jugular vein of a rabbit will cause a quite distinct rise of blood-pressure, whereas I have not been able to induce glycosuria by intravenous injection of 1 c.c. or even 2 c.c. of a 1 : 1,000 solution, that is, up to and including the lethal dose; subcutaneously, on the other hand, less than 1 mgrm. per kilogram body-weight cannot be relied upon to cause glycosuria, although a smaller dose produces widespread local anæmia. If, then, as is suggested by the action of tyrosinase, rapid oxidation of a part of the adrenalin molecule in the blood accounts for the loss of power to cause glycosuria, how is the glycosuria after subcutaneous injection brought about? Injected under the skin, adrenalin comes at once in contact with sympathetic nerve-endings, stimulation of which is its characteristic, and so possibly by way of the ganglia an impulse may be conveyed to the centre regulating the amount of sugar in the blood. If this suggestion were correct it might be possible to prevent glycosuria after subcutaneous injection of adrenalin by occupying the sympathetic ganglia and nerve-endings with some other substance and so preventing the access of adrenalin. Dixon has shown that apocodeine is such a drug and that it prevents the rise of blood-pressure after administration of adrenalin. I find, further, that if apocodeine is given to a rabbit and immediately afterwards a dose of adrenalin subcutaneously no glycosuria follows.

It may be further noticed, in support of the explanation suggested for the fact that adrenalin administered intravenously does not cause

glycosuria, that adrenalin injected under the peritoneum causes both a rise of blood-pressure and glycosuria; here the conditions for ready oxidation are limited, whereas sympathetic endings are plentiful. Further, the rise of blood-pressure after peritoneal injection is slower in attaining the maximum and falls to normal less precipitously than after intravenous application, indicating a slower destruction—i.e., oxidation—of adrenalin in the peritoneum. In this connexion it is interesting to observe that tyramine intravenously administered, in correspondence with its greater resistance to the action of tyrosinase, causes a more prolonged rise of blood-pressure and a less sudden fall to normal than is the case with adrenalin, thus indicating that the destruction of tyramine (probably by oxidation) proceeds less rapidly in the blood than does that of adrenalin.

Briefly to sum up the results of these investigations: Potato-tyrosinase so alters adrenalin that both the power of causing rise of blood-pressure and that of producing glycosuria are lost. It is probable that the hydroxyl groups of the ring form one of the points which the tyrosinase attacks. The pressor and the glycosuric powers of adrenalin are so situated in the adrenalin molecule that the one may be lost and the other retained. This takes place when adrenalin is injected intravenously. There is, then, rise of blood-pressure but no glycosuria. On the other hand, although there is no rise of blood-pressure after subcutaneous injection, still the pressor property is not at once lost, for there is constriction of blood-vessels in the injection area, and this continues for an appreciable time. The loss of the power to produce rise of blood-pressure occurs on the way from the subcutaneous tissues to the blood-stream. These facts and, further, the very great difference in the dilution of adrenalin at which the glycosuric and pressor powers are active seem to suggest that these two powers are connected with different points in the adrenalin molecule.

On the other hand, there are two groups of cells upon which adrenalin acts, namely, (1) the vasomotor endings in the blood-vessels, and (2) certain cells in the subcutaneous tissue which must in some way be linked up to the *piqûre* or sugar centre. As these two groups of cells have different functions it is probable that their physico-chemical constitutions are also different.

We may then, I think, justifiably assume that in the adrenalin molecule there are two points: the one is the key to the vasomotor lock, the other to the *piqûre* lock. Both these points must be readily accessible to the action of tyrosinase. To adopt Ehrlich's terminology

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we may think that for pharmacological purposes the adrenalin molecule contains two haptophore groups: one with a specific attraction for vasomotor nerve-endings, the other for nerve-endings connected to the sugar centre. But these groups are deprived of their specific haptophore capacities by oxidation.

The blood-pressure-raising power of tyramine is also destroyed by tyrosinase, but more slowly than is the case with adrenalin, and the blood-pressure curve of tyramine is accordingly more prolonged and less abrupt than that of adrenalin. Up to the present I am not aware that anyone has found glycosuria after subcutaneous injection of tyramine; my own investigations show that up to 0.04 gr. per kilogram no sugar occurs in the urine of rabbits.

Note.—A full report of the experiments alluded to above will appear shortly.

DISCUSSION.

The PRESIDENT (Professor W. E. Dixon, F.R.S.) said that the subject of adrenalin was one of interest to everybody. There was one point that impressed him particularly in Dr. Ransom's paper; this was his statement that adrenalin administered by a vein did not cause glycosuria, but that administered subcutaneously it did. The action in the two cases, according to the paper, was entirely different. Dr. Ransom stated that if adrenalin was put under the skin it excited the sympathetic nerve-endings and produced an effect on the glycosuric centre in the medulla, but that glycosuria was not produced in the case of injection into the vein. The speaker did not think that adrenalin put in the blood could act essentially in a different way from hypodermic injection; he suggested that the absence of glycosuria after intravenous injection might be explained by constriction of the renal vessels.

Dr. T. R. ELLIOTT said that it struck him as rather surprising that adrenalin injected intravenously should have no effect in producing glycosuria. Experiments were required to learn to what extent renal excretion in general was diminished. He thought Dr. Ransom said that an excess of sugar appeared in the blood, so that at any rate the intravenous injection liberated sugar. The non-appearance of glycosuria might be due to failure of urinary flow, or again it might be associated with a toxic action of adrenalin on the kidneys. It was well known that the drug produced a fatty renal degeneration. The suggestion that adrenalin, given intravenously, had no effect in producing glycosuria ran counter to the views lately put forward in France in connexion with the "glycosuria puncture" theory. It was held that if the Claude Bernard puncture were made subsequently to excision of the suprarenals glycosuria did not supervene. The speaker had been able to some extent to confirm the puncture experiment by proving the control through the splanchnic nerves of

the secretion of adrenalin from the suprarenal glands. But underlying all this was the assumption that adrenalin liberated in the blood could produce glycosuria. If Dr. Ransom's experiments contradicted that, then the whole explanation fell to the ground, and it was very important to have the matter settled one way or the other.

Dr. H. H. DALE said that he had been greatly interested in Dr. Ransom's suggestion that the action of adrenalin on the sympathetic nerve-ending on the one hand, and its action in producing glycosuria on the other hand, might be associated with different groups in the molecule. It ought to be easy to test that point since so many substances were now available lying in its immediate chemical neighbourhood. He imagined that by examining a series of these substances for the two types of action some result might be arrived at. That work had already been carried out to a great extent as regards pressor action, but there remained to be investigated the varying degrees in which these substances produced glycosuria. There were no definite statements published on that point so far as he was aware, but he thought it possible that the different groups of the molecule were responsible for the different effects.

Professor A. R. CUSHNY, F.R.S., remembered that a few years previously he had tried to get glycosuria from intravenous injections of adrenalin and had succeeded. The injection was not made in the ordinary manner, but a very dilute solution was infused into the vein for something like half an hour, and then glycosuria came on. But he saw at once that there was a difficulty underlying these experimental conditions, because diuresis appeared, due to the saline; and he could not be quite sure whether it was adrenalin glycosuria or saline glycosuria. He had always supposed that the failure of adrenalin to cause glycosuria when injected intravenously was due to the contraction of the renal vessels. An analogy to this was the failure of secretin to cause a pancreatic secretion when adrenalin was injected at the same time. The question might be tested, however, and he would like Dr. Ransom's views as to whether, when he antagonized the subcutaneous injection of adrenalin by an intravenous injection of adrenalin, nicotine could be substituted for the latter.

Dr. RANSOM, in reply, said that although intravenous injections of adrenalin did not cause glycosuria, they did produce some hyperglycaemia; one explanation was that adrenalin intravenously injected did not raise the sugar contents in the blood up to a sufficient point in rabbits—and it was important to remember that the experiment was carried out with rabbits—above the assimilation line. He thought that Dr. Dale's suggestion might be carried out in some future experiments, and an attempt made to prove what part of the molecule was associated with glycosuria. In reply to Professor Cushny, he had had some difficulty with regard to nicotine, but he was able to use apocodeine—a practically similar drug—and found that it did prevent the occurrence of glycosuria. In some future experiment he would see what nicotine would do, but probably the two actions corresponded very closely. If a large quantity of saline was allowed to run in with the injection one got, of course, glycosuria.

Urinary Antiseptics: An Experimental Investigation.

By A. R. JORDAN, M.D.

A URINARY antiseptic is a drug given by the mouth to disinfect the urine. A large number of drugs being secreted in the urine exert a mild antiseptic effect, but it is only those of practical value in this respect to which the name of urinary antiseptic should be applied, while certain drugs which merely increase urinary acidity are of such importance in association with the urinary antiseptics that they should be included in the same category. Now, while many of these drugs have an established place in therapeutics, but little is known as to their relative power as antiseptics in the urine, and still less as to their relative efficiency against different micro-organisms. It is obvious that a good deal upon these points might be learnt by investigating the growth of micro-organisms in the urine incubated in tubes after it is passed, and observing the effect in preventing or retarding the growth when the different antiseptic drugs have been taken by the mouth. It was upon these lines that this investigation was made. First of all as to methods. The micro-organisms I selected for investigation were naturally from groups which commonly affect the urinary tract. Those which rarely occur were discarded, while it is unfortunately impossible to work with the tubercle bacillus and the gonococcus, since the difficulty of cultivating them is such that no evidence could be gained from any failure to grow them.

I therefore limited myself to the study of (1) putrefaction; (2) the growth of *Staphylococcus pyogenes aureus*; (3) that of *Bacillus coli*. This latter organism is of special interest in connexion with "colibacilluria." As to the drugs, I used acid sodium phosphate to increase and potassium citrate to decrease the urinary acidity, while the urinary antiseptics proper which I have so far investigated are urotropine, sandal-wood oil, santalol salicylate or santyl, salicylic acid, ammonium benzoate, and benzoic acid.

I made use of my own urine throughout these experiments. It was tested before and after the work, and found to be "normal" to the ordinary clinical tests. Complete twenty-four-hour specimens were collected and used, and also "morning specimens"—i.e., specimens

passed on getting up, before breakfast—and I may here mention that the morning specimen bears a constant relation to the twenty-four-hour specimen as far as this type of work is concerned, and it is, of course, a good deal easier to collect it. The various drugs I took by the mouth, taking about the ordinary doses in use in practice, and taking them for a day or two before any specimen of urine was tested.

As regards the study of putrefaction, I incubated the fresh urine as passed in chemically clean, but unsterilized, tubes: in which case it undergoes putrefaction. To investigate the organisms in pure culture it was necessary to obtain sterile urine. I found that the only reliable and practical way of doing this is to filter the urine through a Pasteur-Chamberland filter. Boiling is inadmissible, since the composition is liable to be altered. I used an apparatus in which the specimen of urine could be filtered and collected in a sterile receptacle, and specimens drawn off at intervals as required. These specimens were received in sterile tubes, incubated for a period to make sure that nothing was growing in them, and then sown with the staphylococcus or *Bacillus coli*, which thus grew in pure culture and in urine alone.

In the determination of acidity I used the only method which is possible for clinical purposes or for an investigation such as this, where hundreds of determinations have to be made, namely, direct titration against an alkali. This method does not, of course, give the true acidity of a mixture of acid salts, but the results are strictly comparable, which is all that is here required. I took as an arbitrary standard a degree of acidity which is determined as follows: 10 c.c. of urine are diluted ten times and titrated against decinormal soda, using phenolphthalein as indicator; the first definite change of tint being taken as the end-point. The number of cubic centimetres of soda are then taken as the measure of acidity, after a correction has been made for the specific gravity. It was pointed out by Joulie that in determination of urinary acidity a result is required in terms of the total solids, not of the bulk of liquid, and that in consequence a correction must be made so as to reduce urines of different specific gravities—i.e., different degrees of dilution—to a common measure. This was taken as a specific gravity of 1020, and so the number of cubic centimetres of soda required was multiplied by twenty, and divided by the number beyond 1,000 in the specific gravity of the specimen in question, and the resulting figure was taken as its acidity. Thus, suppose a specimen of specific gravity 1015 to be estimated, and that 10 c.c.

requires 2.8 c.c. of decinormal soda to neutralize it, the acidity is

$$\frac{2.8 \times 20}{15} = 3.9.$$

Determined by these methods, and measured by the standard just described, I find that the acidity of twenty-four-hour specimens, and morning specimens, of the urine is pretty constant. The variation in casual specimens obtained during the day is, of course, enormous, and and is of no significance or value whatever. The fact that a casually obtained specimen is alkaline, for instance, is no evidence at all that the twenty-four-hour specimen will even be of low acidity. Such alkaline specimens are normally secreted after meals, but may be *passed* just before the next meal. I tested the morning and the twenty-four-hour specimens almost daily for five weeks, and found that the average of the morning specimens was 4.3 degrees of acidity, and the extreme limits from 3 to 5.5, while that of the twenty-four-hour specimen was 3.9, the variations being between 3 and 5.

By taking reasonable doses (30 gr. three times daily) of acid sodium phosphate the acidity could be just about doubled (morning specimen 9, twenty-four-hour, 7.9), while with potassium citrate (1 dr. three times daily) the urine was readily made alkaline to an extent corresponding to -2.5 degrees of acidity. These results correspond closely to those of Hutchison, obtained in an investigation of drugs which increase urinary acidity.

Before any results could be arrived at in connexion with the urinary antiseptics it was necessary to determine with accuracy the conditions of growth of these organisms in normal urine, and the effect of variations in acidity and alkalinity alone, these latter factors being of the utmost importance. When a urine of average acidity is allowed to putrefy in the incubator at body temperature it becomes alkaline in twenty-four hours, and is giving off free ammonia in two to three days. Urine which is alkaline when passed putrefies rapidly, while the putrefaction of urine of high acidity is considerably delayed.

A number of experiments were made with a view to determining the effect of the degree of acidity upon putrefaction, with the following results:—

It was found that urine which is alkaline when passed putrefies within a few hours, so that in twenty-four hours it is cloudy, foul-smelling, and giving off free ammonia. That with an acidity of 3 to 4 this change is delayed for thirty-six to forty-eight hours; that with an acidity of 8 or 9 it takes three days; and that it cannot be delayed

beyond four or five days by any increase of acidity which can be produced in the body. In the experiments with *Staphylococcus pyogenes aureus*, tubes of filtered urine were taken and sown with staphylococcus from a young agar culture. The tubes were then incubated at body temperature. In this way the staphylococcus is found to grow very readily in urine and is seen as a deposit of minute whitish granules which tend to adhere to the sides of the tube. It breaks up urea, giving rise to ammoniacal fermentation, but the characteristic foul smell of advanced putrefaction is generally absent. Its growth is favoured by alkalinity, and is delayed by acidity in the same manner as in putrefaction. The time of the first appearance of free ammonia, as in the case of putrefaction, was taken as the gauge of the rate of growth, and similar experiments to the putrefactive ones were performed. The only differences of importance are that the staphylococcus is a little more active, and the experiments more constant, than those with the mixed organisms of putrefaction.

The *Bacillus coli* was grown in sterile urine in the same way as the staphylococcus. It grows very readily and appears as a fine, cloudy deposit which renders the urine uniformly turbid. On shaking or stirring, peculiar glistening swirls are seen, and these are not present in cloudy putrefying urine, nor have I observed the appearance in connexion with any deposit or substance in urine except with bacteria of the coli group and with *Bacillus typhosus*. The *Bacillus coli* is sometimes seen in urine joined end to end, forming a long spirillum-like structure, which in a hanging drop worms its way among the normal motile bacilli. Sown back to agar the bacillus assumes its normal form, and these curious forms appear to occur more frequently in old growths in urine. In urine made artificially many times more acid or more alkaline than occurs in the body, the *Bacillus coli* will grow; and, despite what is said to the contrary, no marked differences are observed in its rate of growth, whether the urine be acid or alkaline. The *Bacillus coli* does not cause alkaline fermentation, and in consequence it is impossible to obtain any such simple indication of its rate of growth as with the other organisms. I therefore made the simple observations that either (1) the organisms grew readily, (2) grew with difficulty, or (3) grew not at all. Until limits of acidity and alkalinity beyond those which occur in the body were reached it was impossible to appreciate any differences in the rate of growth. It is possible that the statement often made that its growth is inhibited by alkaline urine is due to an erroneous assumption from the fact that the bacillus, when growing

alone, tends to occur in acid urine only; such being the case because urine is normally acid and *Bacillus coli* has no tendency, as most of the other bacteria have, to make it alkaline. At any rate, I found no evidence in favour of this assertion.

THE EFFECTS OF DRUGS.

(I) *Urotropine.*

Hexamethylenetetramine, commonly known by the trade name of urotropine, was discovered by Butlerow in 1860 as a chemical substance, and introduced as a drug in 1894 by Nicolaier. It was first suggested as a solvent for uric acid in the same way as was piperazine. The use of both these drugs as solvents of uric acid in the body is now discredited, but the action of urotropine as a urinary antiseptic is established. The fact that urotropine is synthesized from formaldehyde, and readily yields that substance on boiling with acids, suggested that its action was due to the liberation of formaldehyde in the urine. Nicolaier, in his early papers on the subject, showed that the disinfecting power of urotropine in the urine varied a good deal with temperature and other conditions, and he expressed the view that the action of the drug was due to the formation of formaldehyde. Caspar demonstrated formaldehyde in the urine of certain patients taking urotropine. Citron considered that the formaldehyde was present as a loose soda compound. Cotyl and Salus came to the conclusion that the antiseptic action was due to urotropine itself, and not to formaldehyde. Cammidge failed to find formaldehyde in the urine, and concluded that urotropine does not act by its formation. An excellent summary of the whole subject to the year 1905 will be found in a series of papers by Guiard.¹

The first series of experiments which I made with urotropine were done on the lines already indicated to determine its power as an antiseptic. The urotropine was taken in doses of 10 gr. three times daily alone, and in conjunction with acid sodium phosphate and with potassium citrate. In this way specimens of "urotropine urine" of different acidities were obtained, while in addition other specimens of intermediate and higher degrees of acidity were got by the method of direct addition (that is, direct addition of known amounts of sodium bicarbonate and acid sodium phosphate). The results were as

¹ *Ann. d. mal. org. génito-urin.*, Par., 1905, i, pp. 481, 641; ii, pp. 997, 1121, 1281, 1461.

follows: In alkaline urine the presence of urotropine made very little difference. The rate of putrefaction and the growth of staphylococcus were possibly slightly delayed, that of *Bacillus coli* was apparently unaffected. As the acidity increases the action of the urotropine becomes more and more obvious. At about 3.5 (i.e., the average acidity of normal urine) this action is so considerable that putrefaction takes a week or more. Staphylococcus is similarly delayed. *Bacillus coli* grows with difficulty. When the acidity reaches the neighbourhood of 5 to 6 (i.e., a high, but readily produced, degree of acidity) the antiseptic power of the urotropine becomes absolute, and no organism will grow in such urines; they remain indefinitely sterile. The power of urotropine in these acid urines is extremely striking, and in marked contrast to its complete inefficiency in alkaline ones.

These experiments can only be explained by the assumption that in the urines of higher acidity there is present an antiseptic of considerable power which does not exist in the urines which are alkaline or of low acidity.

The degree of antiseptic power of these acid urines was to some extent ascertained as follows: It was found that when urotropine urine of acidity 7 was added in varying proportions to normal urine of acidity 4, one part of this urotropine urine with nine parts of the normal urine was sterile when incubated. Now, in these experiments 30 gr. of urotropine were taken in the twenty-four hours, and about 50 oz. of urine were secreted during that time. Not all, but probably the greater part of the 30 gr., is contained in the 50 oz. of urine; so that the strength of the substance secreted in the urine cannot be above 1 in 1,000, and is probably less; and this, further diluted to the extent of 1 in 10, is, as we have seen, sufficient to prevent putrefaction. I found that if carbolic acid be added to urine to stop putrefaction, about 1 in 800 is required for the purpose; so that the antiseptic substance in acid urotropine must be at least ten times as powerful as carbolic acid. Moreover, Mosso and Paleotti have shown that if formaldehyde be added directly to urine it stops putrefaction when of a strength 1 in 10,000, and has a definite antiseptic effect when present 1 in 50,000; so that it is obvious that the substance present in acid urotropine urine corresponds closely in antiseptic power with formaldehyde, and we have then very strong presumptive evidence in favour of formaldehyde.

It remained to demonstrate the presence of formaldehyde in urotropine urine, and, if possible, to determine the conditions of its

formation. It is upon a failure to do this that the workers who have come to the conclusion that urotropine does not act by the formation of formaldehyde have based their views. Cammidge showed that 5 per cent. of urotropine in neutral solution was required to exert the same antiseptic power as 0.08 per cent. of formaldehyde. It is obvious which of these figures corresponds most nearly to the maximum possible strength of the substance present in a urotropine urine with antiseptic power; yet Cammidge concluded from a failure to detect it chemically that no formaldehyde was present. He used as tests for formaldehyde the reduction of Fehling's solution, the resorcin test, and Schiff's rosaniline reaction. I repeated some of his experiments, with results corresponding to his. He does not appear to have realized in how small an amount the formaldehyde would be, if present, for he mentions the fact that urotropine urine never smells of formaldehyde as evidence against its presence. A solution of 1 in 10,000, which would exert quite a powerful antiseptic action, as we have seen, has, of course, not the slightest smell. Moreover, none of Cammidge's tests, if tried upon a 1 in 10,000 solution of formaldehyde, are positive. There is, however, an extremely delicate test which will readily direct 1 in 200,000 formaldehyde, or even less. This is the phloroglucin test. A 1 per cent. solution of phloroglucin with 25 per cent. of alcohol is made with distilled water, and a little strong caustic soda solution added. A few drops of this gives a bright cherry-red colour with solutions of formaldehyde. In testing for small amounts, the solution should be added slowly, and the colour appears in a few seconds, and fades after a time, probably by reason of the combination of the formaldehyde and the soda. The test solution must be fresh. With this test I have never failed to detect formaldehyde in acid urotropine urine. A distinct red colour is produced on adding the test fluid directly to the urine, which is not produced in normal urine or in alkaline urine containing urotropin. The demonstration may be made more obvious by distilling the urine *in vacuo* at body temperature, and testing the distillate, when a bright cherry-red colour is produced. Boiling is, of course, inadmissible, since formaldehyde might then be produced by the heat. I therefore regard the presence of formaldehyde in acid urotropine urine as demonstrated. Finally, a series of experiments were made to elucidate the conditions under which formaldehyde is formed in urotropine urine. The results were as follows:—

Broth Culture Experiments with Urotropine.—Broth cultures to

which drugs had been added as described were infected with the staphylococcus and incubated for twenty-four hours.

Drugs added to culture	Result
(1) Urotropine, 1 in 20, alone	No growth
(2) Urotropine, 1 in 100, alone	Grew slightly
(3) Urotropine, 1 in 20, with trace of NaHCO_3	Grew slightly
(4) Urotropine, 1 in 300, with trace of NaH_2PO_4	No growth
(5) Urotropine, 1 in 1,000, with trace of NaH_2PO_4	No growth

These experiments demonstrate that outside the body the addition of a trace of an acid salt to urotropine will enormously increase its antiseptic power. They also show that in neutral solution a strength of 1 in 20 will inhibit growth, but that this property is destroyed by the addition of alkali; an explanation of this fact is given later.

Chemical Experiments.—By means of the phloroglucin reaction not only can very small amounts of formaldehyde be detected, but, in addition, from the depth of colour a rough indication of the strength of the solution can be obtained. For this purpose the test is applied and the colour matched by adding the same amount of phloroglucin solution under identical conditions to solutions of formaldehyde of different known strengths. When the colour is identical the strength of the formaldehyde may be assumed to be nearly so. In this way a rough quantitative estimate is obtained.

Experiments.—A solution of urotropine in distilled water of strength 1 in 1,000—i.e., about the strength in which it occurs in urine—was made up, and samples of it were incubated at body temperature for twenty-four hours:—

(a) In neutral solution it was found that the slightest trace of formaldehyde was liberated, probably about 1 in 200,000.

(b) In solution with a small amount of acid sodium phosphate, or a trace of a mineral acid, a strong reaction was given, the colour indicating a strength of about 1 in 10,000.

(c) In solution with a small amount of sodium bicarbonate or other alkali no reaction is given, even after prolonged incubation. This, of course, explains the differences in the behaviour of tubes 1 and 3 in the last described broth culture experiments.

(d) Lastly, if a solution is acidified, incubated, and gives the reaction indicating about 1 in 10,000 formaldehyde, and to it is then added sufficient sodium bicarbonate to make it alkaline, together with a slight trace of ammonia, after twenty-four hours' incubation it fails to show

the least trace of formaldehyde, and all the urotropine has been reconstituted.

It will be seen that these chemical experiments are in every respect consistent with those in which the actual effects of urotropine as a urinary antiseptic were investigated, provided that it be accepted that its powers are due to formaldehyde. Urotropine in solution is a comparatively unstable substance. In acid solutions it tends to disintegrate into formaldehyde and ammonium compounds. In alkaline solution the reaction tends the other way. Various factors—the dilution, the time allowed, and above all the temperature—will affect these reactions, but from a pharmacological point of view one is only concerned with these factors as they occur in the body when urotropine is being given as a drug, namely, with a dilution of 1 in 1,000 or less, and with effects taking place during a number of hours at a temperature of about 37° C. If these conditions are observed, it is found that urotropine in neutral solution disintegrates, yielding formaldehyde to a very small extent, namely, about 0.01 per cent. In alkaline solution no dissociation occurs. In acid solutions the percentage of urotropine which breaks up increases considerably, in a degree varying as the acidity, so that with an acidity corresponding to that of strongly acid urine about 10 per cent. of the urotropine present is split up into formaldehyde.

It has been shown that these processes occur in urine when urotropine has been taken, and that the antiseptic power of the drug runs parallel with, and can only be explained by, the amount of formaldehyde present. So that the object in giving urotropine as a urinary antiseptic is to exhibit formaldehyde in the urine, and to keep this in view constitutes, I believe, the key to the correct use of the drug.

(II) *Sandal-wood Oil.*

Sandal-wood oil has largely superseded copaiba and cubebs, and is generally reputed to be the most efficient of the essential oils. It contains two substances allied to the sesquiterpenes, santalol and santalal. In the last few years these substances, or combinations of them, have been put upon the market under the names of gonosan, santyl, &c. Santyl, which is santalol-salicylate, is highly praised from a clinical standpoint, and in consequence some experiments were done with it to compare its efficiency with that of the crude oil.

Sandal-wood oil, like most other essential oils, is excreted in the

urine partly unchanged and partly as a compound of glycuronic acid. Its reputation as a urinary antiseptic is not great, though it is acknowledged to be of value in the treatment of gonorrhœa. It would seem that here it must act as an antiseptic, though some writers regard its action rather as an "astringent" to the mucous membrane, because in cases of gonorrhœa which are benefited by sandal-wood oil other and more powerful antiseptics are said to be of little avail. This astringent speculation is nonsense; none of the essential oils exhibit astringent properties. Urotropine has not been given a full trial; Leedham-Green found it useful in certain stages of the complaint.

Experiments with Sandal-wood Oil.—The sandal-wood oil was taken in gelatine capsules in doses of 20 minims three times a day, and twenty-four hour specimens of the resulting urine were used. The acidity of the specimens was varied by the method of direct addition (vide supra). The results were as follows: Against putrefaction the action was feeble. Alkaline urine putrefied as readily as it does without sandal-wood oil, while in the acid urine the only effect was to rather more than double the time required to putrefy. The *Bacillus coli* was practically unaffected; it grows readily and freely in sandal-wood oil urine of all acidities. It was, however, very different with the staphylococcus. Its growth in alkaline urine was delayed to six or seven times the normal period; in moderately acid urine it took nine days to render the urine ammoniacal, while in highly acid urine it was barely growing at the end of a fortnight. In other words, here was quite a marked antiseptic effect upon staphylococcus and practically none against *Bacillus coli* or putrefaction.

This selective action of the drug upon a particular organism was so unexpected, that to exclude the possibility of error all these experiments with the staphylococci were repeated, using controls of normal urine of corresponding acidities, but similar results were obtained and there seems no question of the accuracy of the observations.

It was noticed that in the sandal-wood oil urine which was undergoing putrefaction, while there was a delay in the appearance of free ammonia, the cloudiness of commencing putrefaction appeared fully as early as it does in normal urine. It may be suggested that this is due to a restraining influence of the drug on the putrefactive cocci rather than the bacilli, if, as seems likely, we assume that the cocci are the chief agents in breaking up urea. Moreover, the fact of the value of sandal-wood oil against the gonococcus would be explained if we assume this selective action to extend to cocci generally. However

this may be, there seems to be no doubt that sandal-wood oil has a considerable degree of power in preventing the growth of staphylococcus while towards the other organisms it is almost inert.

Experiments with Santalol Salicylate ("Santyl").—To obtain some idea of the comparative values of sandal-wood oil, and of its derivative santalol salicylate (santyl), some specimens of urine after taking the latter drug were allowed to putrefy and the results compared with those obtained with the crude oil. It was taken in doses of $\frac{1}{2}$ dr. three times daily. The results were slightly better than those with the crude oil, but since the dose was much larger it must be concluded that santalol salicylate has, if anything, a feebler action than has sandal-wood oil; however, the drug can be given in larger doses, and it is less unpleasant to take.

(III) *Salicylic Acid.*

Salicylic acid was chosen as the first representative of those coal-tar products which have a urinary antiseptic action. Of these, salol, phenyl salicylate, is reputed to be the most powerful, but since it has a double action, due to its two constituents, it seemed not to be so suitable for experimental purposes. Salicylic acid is secreted in the urine as salicyluric acid and as sodium salicylate. In an acid urine some of this sodium salicylate is split up, yielding the free acid. As a pure antiseptic, it probably does not matter much in what form salicylates are taken, but the acid itself has the reputed power of increasing the urinary acidity to some extent; and it was among many drugs used for this purpose before the introduction of acid sodium phosphate. With a view to getting some idea of this secondary action, I took salicylic acid instead of any of its derivatives.

It was taken in doses of 20 gr. three times daily. Twenty-four-hour specimens of urine were used. No appreciable increase in the acidity of the twenty-four-hour urine resulted. The twenty-four-hour specimen with which the pure culture experiments were made had an acidity of 3.5—i.e., slightly below the average. Hutchison, who investigated this point, found that the acidity was slightly increased. Possibly, had the drug been taken for a longer period the average acidities would have shown some increase; but my result shows that this action is very feeble and quite insignificant.

For investigating the antiseptic action, experiments were done of the same kind as with the other substances. The results were as

follows: Against putrefaction the salicylic acid had quite a decided effect, prolonging the time required for ammoniacal fermentation to about three times its normal length. With the staphylococcus the results corresponded—its growth was only delayed to about three times the normal period; though in urines of very high acidities it grew very badly, and the delay was greater than this. *Bacillus coli* did not grow quite so well in the salicylic urine as in normal urine, but there was very little effect upon it.

(IV) *Benzoic Acid and Ammonium Benzoate.*

These drugs, like salicylic acid, are used as urinary antiseptics, and also for the purpose of increasing urinary acidity, for both of which purposes their reputation is higher than that of salicylic acid. The increase in acidity is, of course, due in part at least to the formation of hippuric acid. I found that this increase in acidity is quite a real and decided one. After taking 15 gr. of ammonium benzoate three times daily, the acidity of the "morning specimens" was raised to between 5 and 6, the average being nearer the latter, and one specimen at 6.5 being obtained. Benzoic acid does not yield any higher degrees of acidity than does ammonium benzoate, and I could not find that it possesses any advantage over the salt. The benzoates are thus second only to acid sodium phosphate in raising urinary acidity (this was first demonstrated by Hutchison in the work referred to above); and it would naturally seem that by taking the two salts in conjunction, a urine of acidity representing the sum of the increase due to each might be got. This, however, appears not to be the case. The resulting urine has only an acidity such as might be obtained from acid sodium phosphate alone. I have twice confirmed this fact, but can suggest no explanation of it. As regards the antiseptic power of the benzoates, alkaline benzoic urine appears to possess no antiseptic power worth speaking of. It putrifies, and the organisms grow in it almost exactly as in normal alkaline urine. As the acidity increases a retarding effect upon putrefaction and upon *Bacillus coli* becomes apparent; so that with a moderate acidity putrefaction takes three or four days, and *Bacillus coli* grows not freely. With a high acidity (7 or 8) putrefaction is much delayed, that is to say, though the urines become cloudy, and organisms are growing in them, alkaline fermentation does not take place, even after ten days or so. The *Bacillus coli* in these highly acid benzoic urines grows very sparsely—there is a

definite and decided inhibition. The staphylococcus, on the other hand, seems quite unaffected by benzoic urine. A vigorous specimen will render even highly acid benzoic urine ammoniacal in twenty-four hours.

It will be seen that in the case of both benzoic and salicylic acid there is an increase in antiseptic power in the highly acid urines which is greater than can be accounted for by the increase in acidity alone. This is presumably due to the fact that the salicylic or hippuric acids are the chief agents in this power.

CONCLUSION.

In conclusion, I should like to say a few words as to the application of these results. It has been shown that the degree of acidity of the urine in which they are to act is an all-important factor in the efficiency of urinary antiseptics. If the urine is normal, or is infected with an organism which does not produce alkaline fermentation, it can be readily made more acid by giving acid sodium phosphate, until the giving of urotropine in conjunction produces an amount of formaldehyde in the urine which renders it completely and totally inhibitory to the growth of any organism. In short, when the acidity of the twenty-four-hour specimen of urine can be raised above 5, urotropine is for all purposes and against any organisms the best drug. Unfortunately it is only in a limited number of the cases in which disinfection of the urine is aimed at that an acid urine exists. The commonest of these conditions are:—

(1) Where the urine is healthy, but some operation is to be performed upon the urinary tract, or there is some injury of it; here urotropine is used as a prophylactic, and very successfully.

(2) The typhoid bacilluria after enteric; this was the first condition in which the value of urotropine was demonstrated clinically.

(3) In *Bacillus coli* infections of the urinary tract.

In all these conditions urotropine is admittedly the best drug to employ, but there are two points in connexion with it which follow from this work which are, I think, worth mentioning:—

(a) It would appear that there is no object in giving large doses of urotropine since, if the urine is sufficiently acid, 10-gr. doses will keep it sterile, the all-important point is a high acidity; and urotropine should not be discredited unless the twenty-four-hour specimen has been estimated and shown to have an acidity above 5 for some days.

(b) It is widely stated that *Bacillus coli* grows worse in an alkaline than in an acid urine. Of this, as I said, I have been able to obtain no evidence. Upon this assumption, however, it has been recommended that in coli bacilluria, potassium citrate should be given with urotropine to render the urine alkaline. Even if the alkaline urine does have the effect of inhibiting the colon bacillus, it is perfectly certain that it will completely and certainly inhibit any action of the urotropine, which may as well be left out of the prescription.

But while urotropine is absolutely efficient, and several of the other drugs, notably benzoates, quite reasonably efficient in acid urine, it will be noticed that on the results of this work nearly all of them are almost inert in an alkaline urine. Unfortunately it is here that they are, perhaps, most needed. The only drug which had any marked action was oil of sandal-wood, where the staphylococcus was the cause of the alkalinity. If this action extends to cocci generally (which seems probable), I should be inclined to think that it is probably the best drug to *begin* giving in cases of cystitis, with foul ammoniacal urine. In such cases all attempts to make the urine acid with acid sodium phosphate, &c., are useless until the alkalinity approaches somewhere near the neutral point, and it is only then that urotropine, benzoates, &c., begin to act at all. The chief treatment of such cases must always consist in bladder washes, and local surgical measures, but if a drug is given by the mouth, of those I have investigated sandal-wood oil would appear to be the best. The discovery of a substance which would, in alkaline urine, exert something approaching the antiseptic power of urotropine in acid urine would be an immense advance in therapeutics.

DISCUSSION.

The PRESIDENT (Professor W. E. Dixon, F.R.S.) said that Dr. Jordan's paper contained a great deal of interesting matter for discussion. One point which, so far as he knew, they had not appreciated before was that these antiseptics could exhibit a specific influence on special organisms. Dr. Jordan's work was as yet of too limited a character for general conclusions to be drawn as to how far this specificity extended. It would be particularly interesting to know whether there were other drugs having specific effects on different organisms besides the essential oils. He hoped that Dr. Jordan would continue his work in this direction.

Dr. ALFRED L. SACHS said that he had been greatly interested in Dr. Jordan's statement, based on his laboratory experiments, that the action of

urotropine increased markedly in proportion to the acidity of the urine. In his own clinical experience he had found that when he administered urotropine (or preferably helmitol) plus acid sodium phosphate, about 25 gr. of the latter with 10 gr. to 15 gr. of the former, the action of the combination was much greater and more rapid than that of urotropine or helmitol alone. He always prescribed this combination since he had noticed this increased effect, and was glad to have had this point now definitely and scientifically upheld by Dr. Jordan. In those diseases of the urogenital tract in which the parasites were not on the surface, but were subepithelial, he was certain that these urinary antiseptics could have no action. Such was the case in certain phases of tuberculosis, in bilharzia, and in gonorrhœa. In gonorrhœa it was, after all, only in the first stage of invasion that the gonococci were exclusively on the surface. Generally only about five days sufficed for the superficial phase to become a "profunda," and in such a condition he was convinced that none of the antiseptics could possibly render the bacteria innocuous. The only advantage in using the antiseptic in such a case would lie in attempting to prevent the further superficial onward spread of the bacteria and kill off such as were brought up to the surface by means of the leucocytes. Sandal-wood oil was universally used in gonorrhœa, and Dr. Jordan had proved by experiments that it was a urinary antiseptic of value. He (the speaker) was not so sure whether its action as an analgesic was not far more important than that of an antiseptic. He recalled a very acute case of cystitis (*Bacillus coli*), with a temperature of 104 F., and great pain, tenesmus and frequency of micturition, in which one of the sandal-wood preparations—in this case thyresol—had afforded inestimable relief from pain within twenty-four hours. It would be interesting to know if the pharmacologists could explain this phenomenon by supposing the possibility that irritating substances in the urine were enveloped by sandal-wood oil, or if by some chemical process the irritant was turned into a non-irritant. The point as to whether the *Bacillus coli* lived in alkaline urine was one upon which his own experience differed from that of Dr. Jordan, although he (the speaker) had no evidence to prove his contention. One scarcely ever found *Bacillus coli* in alkaline urine, and Dr. Jordan had explained that the reason was that *Bacillus coli* did not cause alkaline fermentation. Well and good, but how was it that *Bacillus coli* was so seldom found in conjunction with staphylococci and streptococci in an alkaline urine, but reappeared as soon as the reaction became acid? It rather looked as though, during the alkaline stage, the *Bacillus coli* was killed off, and that with the acid stage the staphylococci and streptococci went under, the *Bacillus coli* once again being able to thrive and multiply.

Dr. H. C. CAMERON expressed his appreciation of Dr. Jordan's paper, which, he thought, should prove of value in the study of that urinary infection in which there was not the alkalinity to be found in cystitis. Pyelitis was extremely common, especially when one came to search for evidence among bottle-fed infants. When the trouble was taken to examine the urine of such infants the

peculiar liability to this infection was noticed, and there had been a good deal of literature upon it. His general impression was that Dr. Jordan's view ran counter to the prevailing clinical opinion. The speaker imagined that urotropine had been rather under a cloud recently as a suitable drug to prescribe in these cases of pyelitis and similar infection in children, and that the uses of potassium citrate were more insisted on. But the question of the acidity of the urine of these infants had not really been taken into account, and after hearing such a valuable paper one would be more inclined to find out definitely the precise value of urotropine. So much attention had been paid to bacteriology and treatment by vaccines in these infections of the urinary tract that too little interest had been taken in the study of urinary antiseptics.

Dr. H. H. DALE congratulated Dr. Jordan upon a paper of exceptional interest and value. He assumed it was not suggested that these apparent specificities of an antiseptic for a particular organism were peculiar to this group of urinary antiseptics. He gathered that if it was desired to arrive at the value of an antiseptic it was essential to state the organism with which it was being tested. Certain antiseptics were known to be more vigorous in their action on a particular group of organisms and others upon another group.

Dr. JORDAN, in reply, agreed with the President that it was very necessary to do some further work of this kind before arriving at definite conclusions as to specificity. The antiseptic value of sandal-wood had been doubted by Dr. Sachs. It had been described as an astringent, which he thought was quite wrong. There was a general idea that it did good, although it was not given credit as an antiseptic. In his experience it did seem to act as an antiseptic against the staphylococcus, though not otherwise. The question of *Bacillus coli* was an interesting one. He could not say anything very authoritatively in explanation of the fact that the *Bacillus coli* did not grow so well in acid as in alkaline urine. He was quite sure that it would grow in alkaline urine very well, and his statement was merely to the effect that it did not make very much difference, nothing like so much difference as the presence or absence of urotropine made in an acid urine. Dr. Sachs was rather difficult to answer when he described cases in which there were the staphylococcus and the streptococcus but no *Bacillus coli* in an alkaline urine, and then, upon making it acid, the *Bacillus coli* appeared. In most cases of alkaline cystitis there were putrefactive organisms which might be *Bacillus coli*, but this could not be stated with certainty unless special investigation were made. If such a urine then became acid the other organisms would be killed off and the *Bacillus coli* remain. The latter might have been present all along. It was further to be noted that the change from acid to alkaline urine might be good. He had seen a series of cases of bacilluria (*coli*), some of them in infants, published by Dr. J. R. Charles, of Bristol, and one or two of these improved after potassium citrate had been given. This improvement occurring with potassium citrate after urotropine had been given might be due to the change in the environment of the organism. It was quite useless to give urotropine with

potassium citrate, and in so far as urotropine certainly was a valuable drug it was a mistake to give potassium citrate if the effect of urotropine was required. He strongly recommended the estimation of the urinary acidity when urotropine was being given, and until this had been shown to be sufficiently high the latter could not be justly condemned. He believed, in reply to Dr. Dale, that if it were investigated there would be found to be a good deal in the nature of specific action on different organisms. The principle of changing the antiseptic after the organism had possibly become accustomed to it was a good one both in the case of urinary antiseptics and others.

Therapeutical and Pharmacological Section.

January 16, 1912.

Professor W. E. DIXON, F.R.S., President of the Section, in the Chair.

The Causes and Treatment of High Blood-pressure.

By WILLIAM BAIN, M.D.

THE height of arterial blood-pressure depends chiefly upon two factors, namely, cardiac activity and the extent of the peripheral resistance. If the heart's force or rate increases, more blood will be sent into the arteries, consequently there will be a rise of arterial blood-pressure. If the heart's force and rate remain constant, and the constriction of the peripheral vessels increases, there will also be a rise of arterial pressure, because again there will be more blood in the arteries, as it cannot readily pass from them through the constricted arterioles into the capillaries. Constriction of the arterioles usually leads to increase of cardiac action to overcome the resistance; this again is an additional cause of a rise in arterial pressure. In each case the opposite will produce a fall in pressure. The most important of the peripheral areas concerned is the abdominal or splanchnic area. Variations here may be very great, and as the area is a large one, its effect on general blood-pressure may be considerable.

Both factors are under the influence of the nervous system. In the case of the heart impulses received through the vagi have a moderating effect, while those which pass through the sympathetic are stimulating. The blood-vessels, especially the arterioles, are provided with two sets of nerve-fibres—vaso-dilator and vaso-constrictor—which carry impulses the effect of which is indicated by their names. In normal subjects there is a balance established between these opposing forces, so that there is produced a cardio-vascular adjustment whereby the various parts of the circulatory machine work harmoniously.

Psychical states, such as excitement or anger, generally induce a rise in pressure. Even the apprehension attending a consultation with a strange physician may raise the pressure 10 to 30 mm. Hg.

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If a drug, or emotion, or the stimulation of any nerve produces a rise or fall of pressure, the investigator has always to put to himself the question, Is the action upon the heart, or upon the peripheral resistance, or upon both? The investigation of this question by experiments on animals is laborious—heart tracings, oncometer tracings, as well as blood-pressure tracings have to be taken. Suppose it is settled that the action of a drug in raising or lowering pressure is cardiac, the further question then arises, Does the drug act on the cardiac muscle, the cardiac nerves, or the centres which control these nerves? Similar questions arise if the effect is a peripheral one, for the inquirer has then to ascertain whether the drug acts on the muscular tissue of the arterioles, or on the vasomotor nerve-endings, or the vasomotor centre. As before stated, it is usually in the splanchnic area that such variations occur. Using the modern resources of the laboratory which enable the pharmacologist to answer such questions in a fairly satisfactory way, it has been ascertained that adrenalin, one of the most powerful of pressor substances, acts on the vasomotor nerve-endings, and that pituitrin acts most probably upon the plain muscle-fibres themselves. In both cases, as is well known, the effect is sufficient to produce a pronounced influence upon the general blood-pressure.

In recent years interest has centred around the physiological action of various organic bases. These are readily obtained from the ultimate cleavage products of proteins called amino-acids (leucin, tyrosine, &c.). If carbonic acid is removed from any of these organic acids, a base is left behind. We shall see that some of these bases are intimately connected with the pathology of high blood-pressure.

The normal systolic blood-pressure in the radial is supposed to vary between 100 and 140 mm. Hg. The diastolic pressure is about 20 to 40 mm. less than the systolic. More trustworthy information is obtained if the two pressures are taken almost simultaneously. I expect medical men would differ greatly regarding the point—the dividing line—at which the pressure ceases to be physiological, and becomes of pathological import. I attach very little importance to the systolic pressure if it is under 155. I exclude valvular disease with established compensation. In these cases a pressure of 150 or 160 is generally desirable.

Before glancing at the causes of increased arterial tension I should like to make two remarks regarding arterio-sclerosis: (1) That the sphygmomanometer readings are apt to be misleading on account of the thickening of the arteries. (2) It has been pointed out by two

careful observers that only in 50 per cent. of the cases of arterio-sclerosis is the blood-pressure above normal. That arterio-sclerosis may exist without the blood-pressure being increased is now generally admitted. On the other hand, it is reasonable to suppose that if all the arterioles are affected, the peripheral resistance must be greatly increased, and the force necessary to overcome this opposing factor must raise the pressure.

What are the causes of the high blood-pressure in man? For some considerable time it has been ascribed to auto-intoxication—to some toxic product circulating in the blood. It was suggested, for example, that there might be an over-action of the suprarenals producing an excess of adrenalin. Broadbent, in 1906, said "the clinical significance of high blood-pressure is generally admitted to be the presence in the blood of some constituent—a glandular secretion or product of metabolism or mineral matter which provokes resistance in the peripheral circulation." Nephritis, puerperal eclampsia, angina pectoris, gout and lead poisoning, are important causes. Another undoubted cause is acute anæmia of the medullary centres in the brain. The condition is fortunately exceedingly rare, and, in discussing the treatment, will be excluded from consideration. In cases of exophthalmic goitre where there is hypertension, I believe it to be due to psychical disturbance.

It has recently been shown that there are substances present in normal urine which, when injected intravenously into animals, produce a rise of blood-pressure. These organic bases to which reference has been made are products of intestinal putrefaction. I have adduced some evidence¹ that these are iso-amylamine derived from leucin, p-hydroxyphenylethylamine derived from tyrosine, and trimethylamine a derivative of choline. In cases of high blood-pressure, these pressor bases are either greatly diminished, or altogether absent from the urine. I have explained elsewhere (*loc. cit.*) that low diet does not account for their marked diminution in many cases of hypertension; hence the presumption is that they are retained in the body, and produce the persistent rise in pressure. It is not my intention to discuss the pathology of arterio-sclerosis, but it may be pointed out that pressor bases circulating in the blood will produce spasm of the arterioles, and that continued spasm of these vessels will inevitably lead to hypertrophy of their muscular coat. If the retention of the pressor bases

¹ "Pressor Bases in Normal Urine," &c., *Lancet*, 1909, ii, p. 365.

in the organism is the chief cause of high blood-pressure, one would expect that a decrease in their formation would be followed by a reduction in the blood-pressure. This, as we shall see presently, does happen. Their formation can be diminished by withholding the food substances from which they are derived, and by inhibiting intestinal putrefactive processes. It is interesting to observe that the bases are absent from the urine of children. They apparently begin to form about the age of 14, and are excreted in normal amounts about the age of 24.

We shall now consider the effect of various diets upon their formation as evidenced by their excretion in the urine.

(1) Vegetables and fruit yield little or none of the bases; consequently, if the increased pressure is due to the retention of the pressor bases these foodstuffs can be taken with impunity in hypertension.

(2) Eggs and fish yield a moderate amount of pressor bases; on chicken diet the yield is more pronounced, while beef and mutton furnish the largest amount. It may be mentioned that my results are practically identical with those of Abelous.¹

If it were shown that by dieting alone the blood-pressure could be kept within normal limits it would be a great gain, for most of the methods in vogue to reduce the pressure are more or less temporary expedients.

During the past summer I treated five cases of high blood-pressure with strong sulphur water and restricted protein diet. I found a difficulty in getting patients to submit to this kind of treatment. Being sent to a health resort, they naturally expected to be ordered both waters and baths. The diet consisted of fruit and vegetables (*ad lib.*), eggs and fish in moderation and fowl sparingly; beef and mutton were forbidden. The result was equally gratifying in the five cases. I will briefly describe two of them.

Mr. A., aged 62. A case of arterio-sclerosis. He complained chiefly of giddiness and fullness in the head. His medical adviser wrote that his blood-pressure was 280 six weeks before he came to Harrogate. There was a trace of albumin in the urine which persisted. When I saw him on June 27 his systolic blood-pressure was 198. He was then put on restricted diet and sulphur water. On July 1 his pressure was 182; on July 10, 160; and on July 17 it was 147. On that date he insisted upon having two Aix douches a week. On July 23 his pressure was 143 and on August 7, 128. I then allowed him a small quantity of beef daily, and he had three Aix douches weekly. On August 22 his pressure was 140.

¹ Abelous and Bardier, *Comptes rend. Soc. de Biol., Par.*, 1908, lxx, p. 560; *Journ. de Phys. et de Path. gén., Par.*, 1909, xi, p. 112.

Mr. B., aged 57. He complained of pain in the upper arms, and a tightness across the chest after walking about a mile. These sensations came on more quickly in cold weather. He felt them first two years ago. He had taken the following mixture regularly for two years: Sod. nitrite 1 gr., pot. iod. 6 gr., glycerine $\frac{1}{2}$ dr., aq. chloroform $\frac{1}{2}$ oz., three times a day. I stopped the mixture. His initial treatment was exactly similar to A's. On September 19, when he began dieting, his systolic pressure was 201; on October 2 it was 152. From that date he had three Nauheim baths a week. On October 25 his pressure was 140. This patient had a remarkably good appetite. He informed me that he had that morning for breakfast—porridge, fish, a couple of eggs and two apples.

The other three patients had no baths, otherwise the treatment and results were similar to A's. The five patients felt greatly improved in health. These facts speak for themselves.

In treating cases of high blood-pressure I generally adopt the following plan: If the systolic pressure is about 200 I usually prescribe nitroglycerine or erythrol tetranitrate for a few days, put the patient on a restricted protein diet, advise strong sulphur water daily, and give him one of the following baths: Aix douche (without abdominal massage or needle douche), Nauheim, liver packs, modified Turkish, electric light bath, D'Arsonval, or a strong sulphur bath. Massage of the back and extremities is helpful, and a moderate amount of outdoor exercise very desirable. The reason why in starting treatment I frequently give nitrites is because there is generally an initial rise of pressure attending bathing operations, either from apprehension, or heat, which might prove dangerous. There are certain patients who cannot take nitrites on account of the splitting headaches they produce. When the nitrites disagree I use either guipsine, or hippurate of ammonia, put the patient on a vegetable diet, and delay bathing for a week. The sulphur water clears out the alimentary tract daily, and is an intestinal disinfectant. Unquestionably the most important part of the treatment is restriction of the diet on the lines indicated. It is necessary to impress upon the patients that they must adhere strictly to the diet sketched out for them until their blood-pressure comes down to normal. A vegetable and fruit diet can be made fairly palatable.

While most practitioners recommend Aix douches as agents for lowering blood-pressure, I have not seen liver packs suggested for this purpose. Yet in certain cases where the hepatic dullness was slightly increased the packs have had a distinctly beneficial effect. This leads me to say that each case should be treated on its merits. Nauheim baths, like the Aix douche, facilitate the peripheral circulation, thereby

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relieving the embarrassed ventricle, and this effect is secured with a lower temperature than in most other baths. What is meant by a modified Turkish bath is that the patient alternately sits in the Russian room and the first hot room, spending a couple of minutes at a time in the former and ten minutes in the latter. Consequently, he is not subjected to a higher temperature than 130° F.

Many practitioners condemn the use of alcohol and tobacco in cases of high blood-pressure. It is a great hardship to be cut off nearly everything that makes life worth living. Providing patients carry out dietetic instructions, I think, if they desire it, they might be allowed to enjoy alcohol and the fragrant weed occasionally.

In the earlier stages of arterio-sclerosis I believe the iodides have a beneficial effect in promoting the absorption of effused material, and in relieving spasm of the smaller vessels, but it is a difficult matter to decide when the arterioles are beginning to become hypertrophied. It is wiser to err on the safe side and give iodides when there is the least suspicion of a pathological change in these vessels. It must be remembered that in administering the iodides we are not attempting to remove the cause of the high blood-pressure. We are merely treating a consequential sequela of hypertension. The iodides do not promote the excretion of the toxic products which produce the vascular changes. When such a drug is discovered the treatment of high blood-pressure will be simplified.

DISCUSSION.

The PRESIDENT (Professor W. E. Dixon, F.R.S.) said that the paper was of such importance and there was so much in it which might be criticized from the therapeutical standpoint that he did not propose to occupy more than a minute or two. The author had shown, he believed, for the first time, that the urine of normal people contained bodies—extractives—which raised the blood-pressure, and that those substances were absent from patients suffering from high blood-pressure. Dr. Bain assumed—for he seemed to have submitted no direct evidence on the point—that the retention of those pressor amines was the cause of the high pressure. He would like the author to clear up the following point: Why should it not be that, in the cases of patients suffering from high blood-pressure (a condition well known to be associated with renal conditions), the kidneys could not excrete efficiently, and that the absence of pressor substances in the urine was one of the results of high blood-pressure, and not the cause of it?

Dr. H. H. DALE said that practically all he had to say about the matter had already been published, largely in conjunction with the President. He

had listened with great interest to Dr. Bain's paper, and there were some points which to him also were somewhat obscure. He had hoped the author was going to give, on the present occasion, more definite evidence than was contained in his hitherto published papers on the identification of these bases. As Dr. Bain said, the pressor action of these extractives from putrid material was first described by Abelous and those working with him, and they succeeded in extracting a base, or mixture of bases, which produced the effect. The identification of the bases producing the effect was made by his colleagues Dr. Barger and Dr. Walpole some years ago. Dr. Bain had applied methods which, in some respects, followed those laid down by Barger and Walpole, in dealing with these bases from the urine, and he (Dr. Dale) supposed that, unless the author had some further evidence to present, his statement that iso-amylamine occurred was made on the evidence that there was a base in the urine which could be shaken out from alkaline solution into ether, and which was volatile when distilled with steam. He also assumed that Dr. Bain's statement that p-hydroxyphenylethylamine occurred in the urine was based on the evidence that there was another base which could be extracted only from neutral solution, or one alkaline with sodium carbonate, into amyl alcohol, or ether, and thus corresponded to p-hydroxyphenylethylamine in its solubilities, as described by Barger and Walpole. But it would be very interesting to hear more evidence on the subject. Abelous pointed out several years ago the existence of a pressor base in the urine, and drew attention to its resemblance to the bases derived from putrid meat. But his analytical data were inaccurate, and he could not identify the bases. The assumed identity was based upon general similarity, without any definite chemical proof. This was the position at present with regard to chemical identification. Trimethylamine had been mentioned as a pressor base in the urine. Abelous had described pressor action with that substance, but he (Dr. Dale) could say that its pressor action was practically negligible. It must be given in very large quantities before any effect was evident, and it did not rank with the other pressor substances; in fact there was no evidence that such action as it had was of the same type. Another factor which Dr. Bain seemed to have overlooked, and which required further explanation, occurred to him. He was ready to be convinced that the bases which had been extracted from urine were those putrefactive amines; such evidence as there was, was in favour of that identification. But there were difficulties in the way which made it the more necessary to have the identification perfect and absolute. Ewens and Laidlaw had dealt with the question of the fate of these amines in the body. It was assumed, and even in health it was almost certain, that they arose in the alimentary canal, where considerable putrefactive action was going on, especially with high protein diet. Ewens and Laidlaw had shown that if large quantities of p-hydroxyphenylethylamine were administered to a dog by the mouth, a physiological action resulted and the result was a rise of blood-pressure, a labouring heart, dilated pupils, erect hair on the back, and general symptoms of sympathetic stimulation, such as resulted from intravenous

injection. But there was no trace of the base in the urine. This fact was explained by the rapid destruction of the substance when perfused through the isolated liver of the rabbit, the cat, or the dog. Ewens and Laidlaw worked chiefly on the rabbit for the purpose, and they found that its liver very rapidly destroyed those bases when perfused through the artificial circulation, converting p-hydroxyphenylethylamine into parahydroxyacetic acid, which was the substance obtained from the urine when p-hydroxyphenylethylamine was given hypodermically or by the mouth. The difficulty was to connect that observation on the lower animals with the appearance of the substances in human urine. Even when administered in quantities altogether outside the range of the quantities in which one could suppose they arose in the intestines, they were destroyed in the liver, and excreted in another form. The difficulty was to imagine why they should appear in the urine of the normal human person. And if that was explained, there was the still further difficulty of explaining why they did not appear in the urine of the person who had high blood-pressure. It was natural to suggest, when one knew of bases arising in the intestine, which, when injected intravenously, caused a large rise of blood-pressure, that these would be a factor in the production of a pathological rise of blood-pressure. But it was known that, even when supplied in considerable concentration to the liver, they were rapidly destroyed, and it was difficult to suppose that at the normal slow rate of absorption in the portal circulation, they could possibly escape the destructive influence of a healthy liver. This suggested that if they really were a factor in the production in these high blood-pressures, possibly the faulty action of the liver had something to do with it. He hoped Dr. Bain would be able to give some more indications as to the method of identifying these bases. This seemed a matter of all the more importance as their presence was not consistent with what one found in animal experiments.

Dr. BEZLY THORNE said that fifteen years ago, when the Schott-Nauheim methods were introduced into this country, he was asked to lecture on the subject before a Midland Branch of the British Medical Association, and, having recognized the danger of too much attention being directed to purely balneological treatment, and the importance of certain factors in the production of cardio-vascular troubles, he made a point of giving to his paper the title "Self-poisoning in Heart Disease."¹ In that paper he pointed out that in a very large number of people suffering from cardio-vascular troubles, and high blood-pressure among those troubles, it was almost invariably found that they were affected with what was falsely called "sluggish liver"; i.e., those patients, were liable—whether constipated or affected with intestinal catarrh—to have pale yellow stools, as the result of gastro-duodenal catarrh. He mentioned this because it had been suggested that the function of the liver was to destroy those amines and other poisons which raised the blood-pressure. Since and before that time one of the first things he did for a person with cardiac trouble, particularly when that was associated with high blood-pressure, was to take

¹ *Lancet*, 1896, i, p. 755.

steps to induce patency of the common bile-duct. Apart from any other treatment, it was almost invariably found that there was a fall in what was commonly called the systolic blood-pressure in consequence of that treatment, and the stools, which had been habitually yellow, became a healthy brown, and lost their putrefactive odour. He wished also to comment on the testimony which Dr. Bain had borne to the value of the Nauheim bath in lowering blood-pressure. That he had done so was the more interesting because in early days it had been maintained that the baths raised the blood-pressure. He believed he (the speaker) was the first to point out that the effect of the baths was to lower blood-pressure. Shortly afterwards Dr. McGregor Robertson, of Glasgow, confirmed that observation with great emphasis. And here lay the kernel of a very important question. A year ago there was a discussion on blood-pressure in the Medical Section, and he then stated that observations on pressure which depended on what was commonly called systolic pressure were not only inconclusive, but in many cases absolutely misleading.¹ The Nauheim bath, for instance, produced arterial relaxation, but did not raise blood-pressure, but what was called the systolic pressure, or obliterating point, went up because the muscular coat of the artery was partly put out of action by vaso-dilatation. That the blood-pressure was not raised could be abundantly proved. With regard to adrenalin, he had been going through some of his cases, taking them just as they occurred, without selection, between December, 1909, and December, 1910, and had an analysis of twenty-three cases. He would quote a few typical cases, and then speak of the net result of the analysis. One was a case of minor epilepsy, of the cardiac variety, in a girl, aged 23. For determining the blood-pressure he used Hill and Barnard's large instrument with three straps on the armlet, which made a great deal of difference in the reading of the blood-pressure. On December 15 the brachial obliteration point, or the point at which the brachial artery moved the needle, was 155 mm.; the radial pulse appeared at 135, and the balance or diastolic pressure was 80. After being put on 7 minim doses of adrenalin for a week the brachial obliteration point had come down 15 mm., the radial point had come down 15, while the balance pressure remained the same. He called attention to this because he submitted that the blood-pressure had not been lowered at all, otherwise the balance pressure would have gone down at the point at which the hydrostatic and pneumatic pressures exactly balanced each other, but there was no change at that grade. Therefore he suggested that the muscular coat of the arteries in this case exercised a buffer action at the obliteration points of the brachial and radial arteries, which prevented the wave going through any longer to 155 mm., and kept it down to 130, and the difference was not a lowering of blood-pressure, but an increase in the buffer action of the muscular coat of the artery. The second case, that of a woman, aged 34, was similar. On October 17 the pulse was 108, and the brachial obliteration point 130, the radial 90, and the balance pressure 80. She was put on adrenalin, and on November 4 the brachial obliteration was

¹ *Proceedings*, 1911, iv (Med. Sect.), p. 78.

reduced 20 mm., the radial had risen 10, and her balance pressure rose 10, and in the interval there had been very slight attacks of vertigo, lasting only a few seconds, and there was no epileptic attack. The pulse settled down to 96. In another case, one of aortic regurgitation with failing compensation, the brachial obliteration point was 180 mm., the radial 160, and the balance pressure 75. After adrenalin treatment had been given the brachial pressure was reduced 10, the radial 10, and the balance pressure had risen to 10 mm. He suggested that the blood-pressure had risen because the balance pressure had gone up 10 mm.: what was called the systolic pressure had come down 10, not because the blood-pressure had fallen at all, but because the muscular coat of the artery had been brought into action. That was the reason for his statement that observations based upon what was called the systolic pressure were inconclusive and even misleading. The last case he would quote was that of a woman, aged 56, with myxædema. She had been taking thyroid extract for two years, and she came complaining of palpitation and dyspnoea. On October 19 her brachial obliteration point was 180 mm., her radial 160 mm., and the balance or diastolic pressure was 100. After taking adrenalin until November 7, her brachial obliteration point had come down to 120—i.e., a fall of 60—her radial point had decreased from 160 to 110, and her balance pressure was 100 to 90, that is, her balance pressure had come down 10 mm., the radial 50, and the brachial 60. He was aware that those data appeared to contradict the ordinary observations as to the effect of adrenalin. The reason he laid emphasis on them was that he thought the effects in laboratory work of hypodermic injections of adrenalin were not the same as the effects of adrenalin given over a long course by the mouth. And he suggested that in adrenalin the profession possessed a very valuable medication, which was capable of increasing the action of the muscular coat of the artery, and so providing a buffer action which prevented the systolic pressure from coming through, not lowering the blood-pressure, but masking it by its muscular and buffer action, and that in so doing it relieved the work of the heart by increasing the peristaltic conductivity of the vessel itself. Reverting to his twenty-three cases, in two there was no change in either of the three grades. In three there was a rise in the balance pressure in the radial, and no change in the brachial obliteration. In three there was a rise in all grades after fourteen days. In five there was a rise in the balance pressure, a fall in the radial and a fall in the obliteration point. In seven there was no rise in the diastolic or balance pressure, and there was a fall in the radial and the obliteration points of the brachial artery. In three there was a fall in all grades.

Dr. ETTIE SAYER said that she had never tested the urine for pressor substances, but quite agreed that toxins of some sort were responsible for the vast majority of high blood-pressure cases. Nevertheless there were occasional cases in which the rise appeared to be solely due to the nervous system, and she would like to instance one as an example. The lady was an actress, aged 58, who came to consult her for headache and giddiness.

She was in the most intense state of excitement and hysteria, raving at a terrific rate about a stage manager who had promised her a part and had then given it to someone else. Her systolic pressure was 236. A dose of high frequency relieved the headache and brought it to 226. Calomel, bromides and nitrites were prescribed. Next day she was worse, the pressure was 240, but treatment brought it to 226. Next day she missed, but on the following she called to say she was quite well; and indeed appeared to be so. She said she had got the part after all, and that her "attack of nerves" had only been due to annoyance. Although she appeared absolutely serene, it was a surprise to find her pressure 140—or 100 less than on the previous day. Two days later she called again. She was now in the same condition as when first seen: something had gone wrong; she had not got the part after all, another "attack of nerves" had come on, with giddiness and insomnia, &c. That evening she went into the country and had some form of apoplectic attack for which the doctor there treated her. She had a furred tongue, constipation and headaches, which might indicate sufficient auto-intoxication to make the arteries hypersensitive to any excitant, but the speaker could not but think that this sort of case illustrated that although pressor substances were probably the main factor, they were not the *only* ones in raising pressure. With regard to diet, she would like to refer to two vegetarians under her care, who had had blood-pressures of 180 to 190. One was an Indian who had always been a vegetarian but who took eggs and purin substances, which Dr. Haig believed could also raise blood-pressure. Both led mentally worrying lives. She would like to hear from the author whether the man who started at 280 and was brought down to 120 was really well then; because in her experience people who had pressure higher than 260 had always had an amount of renal inadequacy which prevented them being brought so low as this without the heart weakening and they themselves feeling bad.

Dr. F. PARKES WEBER alluded to the class of cases with extremely high blood-pressure, in which the great pressure was *secondary* to grave organic changes in the kidneys and cardio-vascular system, and in which spontaneous hæmorrhage in the brain or elsewhere often supervened. In such cases the brachial systolic blood-pressure not rarely exceeded 200 mm. Hg., and could not be lowered to a normal figure by dietetic or any other ordinary means; but if cardiac failure at last supervened as a result of cardio-vascular disease, the blood-pressure might fall spontaneously to an almost ordinary figure as a sign of approaching or threatening death. In this class of cases of extremely high blood-pressure, if one were able by ordinary means to lower the blood-pressure to a "normal" figure, one would kill the patient.

Dr. HINGSTON FOX said that, valuable as were these researches into the effect of certain toxic substances on the blood-pressure, it was important that one's attention should not be diverted in cases of high-pressure readings from the means which had long been found useful. Thus there were many cases of an arterial pressure over 200 mm., and even over 180 mm., in which it was

54 Bain: *The Causes and Treatment of High Blood-pressure*

our duty to use venesection in order to save the patient from the risk of apoplexy. Such cases needed to be kept under observation, and in some of them a periodical bleeding like that which our ancestors practised was a true prophylactic. He knew of cases in which this measure had saved the patient from risk and apparently preserved life. Mercurial treatment, again, had scarcely been mentioned in this discussion, yet, whatever its mode of action, it was very effectual in reducing blood-pressure. The classic case related by Dr. Murray, of Newcastle, in which a patient took 5 gr. of blue pill nightly, for many years with great benefit to his arterial condition, showed how freely this drug might be used when it was indicated.

Dr. BAIN, in answer to the President, said the bases were either absent or greatly diminished in cases of high blood-pressure, and that in such cases a decrease in their formation coincided with a fall in pressure. From these facts he inferred that they were retained in the organism and produced the persistent rise in pressure. It would be difficult to explain on any other hypothesis why there was a fall in pressure coincident with a diminution in the foodstuffs from which these bases were derived. Dr. Dale had referred to the identification of the bases. He (Dr. Bain) had collected 120 litres of urine, and had extracted the pressor bases from the urine by the charcoal method. The work was now in a forward state, and he hoped to complete it in three weeks' time. Dr. Dale had also referred to Dr. Laidlaw's work on p-hydroxyphenylethylamine, with regard to it being destroyed by the liver. In this connexion it was worthy of note that liver packs had a distinct effect in lowering pressure in certain cases of hypertension. He agreed with Dr. Bezly Thorne regarding the misleading impression sometimes produced by taking the systolic pressure without the diastolic. He had no experience of the clinical effects of adrenalin in hypertension. Replying to Miss Ettie Sayer, he said that neurosis did sometimes raise the blood-pressure, but he thought the increase was then only temporary. He had seen cases of high blood-pressure which were ascribed to neurosis, but on examination of the urine it was found that the pressor bases were markedly diminished, therefore he was sceptical about a persistent rise in pressure being due to neurosis. Regarding vegetarians, his experience was that they did not usually confine themselves to vegetable proteins, but took animal proteins, such as milk, cheese, &c. The patient Dr. Sayer inquired about was now in good health. In answer to Dr. Parkes Weber, the highest systolic pressure he had met with was 240 mm. Doubtless most of the abnormally high blood-pressures were due to advanced pathological changes in the arterioles, and, of course, in these cases dieting could only affect the pressure to a moderate or slight extent. He agreed with Dr. Hingston Fox that venesection was an effective, and in a few cases a valuable, agent for lowering pressure, but some patients had an objection to its performance.

Therapeutical and Pharmacological Section.

February 20, 1912.

Professor W. E. DIXON, F.R.S., President of the Section, in the Chair.

The Uses of Tuberculin in Pulmonary Tuberculosis.

An Address Introductory to a Discussion on the Subject.

By ARTHUR LATHAM, M.D.

IN the first place I wish to thank the President and the Council of this Section for their courtesy in asking me to open this discussion. There can be no doubt that such a discussion is required at the present time, for on the one hand we have a school which to my mind may be regarded as placing the value of tuberculin too high and of focusing their attention on this remedy to the exclusion of other important factors in treatment, and on the other we have a school—daily becoming smaller and less important—which denies that tuberculin is of value. The latter view is largely based on the experience obtained when Koch first introduced his discovery, but that experience has subsequently been shown by patient work to have been vitiated chiefly by an improper system of dosage and an improper selection of cases. Both schools have right on their side, but both are too dogmatic in their generalizations. To-day, I take it, we want, not dogmatic statements but a practical and judicial examination of the results or impressions of our individual experience, so as to make others appreciate the fact that the truth concerning tuberculin lies midway between the conclusions formed by the two existing schools. I propose therefore to introduce the subject under a series of headings with the object of facilitating discussion.

THE RESULTS OBTAINED BY TUBERCULIN TREATMENT.

It is held by some that statistical evidence on this point should be conclusive on one side or the other, and so far as statistical results go they show that tuberculin in association with other methods gives better

results than any other known method of treatment. A larger proportion of patients so treated certainly appear to maintain their working capacity for a longer period, whilst it would also appear to be proved that tubercle bacilli disappear from the sputum in a larger proportion of cases treated by this method than with any other method. There are, however, difficulties, some of which I regard as insuperable, with regard to statistical proof in medical problems. It is difficult, if not impossible, to compare the results of one observer accurately with those of another, as the original data are not strictly comparable. For example, our views as to diagnosis differ. Some rely largely, if not entirely, on the presence of tubercle bacilli in the expectoration, some will make a positive diagnosis on signs and symptoms which will not convince others, and some, again, rely in many instances upon a positive reaction to old tuberculin. It may be said in passing that if the problem of pulmonary tuberculosis can be reduced so far as diagnosis is concerned to a positive reaction to old tuberculin, or so far as treatment is concerned to treatment with one or other of the numerous preparations of tuberculin, then in this particular medicine has become an easy art. Certainly if we rely on an old tuberculin reaction as showing the presence of tuberculosis which requires active treatment, we shall have a large measure of success with tuberculin, but our results will be vitiated by the fact that a very considerable proportion of our cases would have shown equally good results by other methods or indeed without any treatment.

Then we are met by the different views of different observers as to what we mean by what is usually expressed by the unfortunate term "an early case." So-called early cases differ largely in their characteristics and as regards their progress. The fact that the disease appears to be of recent origin does not afford a reliable basis on which to calculate results, and I do not think that we shall be able usefully to correlate the results obtained by different observers until we are in possession of a better classification of the different forms or what are called stages of the disease. The best I know is that of Dr. A. C. Inman, to which I hope he will refer, and which is based upon the facility with which auto-inoculation occurs or is produced.

A further difficulty about statistical proof is the difficulty in keeping our patients, and especially our hospital patients, under observation for a sufficient length of time after discharge to form a useful opinion of the real results. There is also the difficulty when relapse occurs of knowing whether the relapse was not inevitable under the sanitary conditions, conditions of work and so forth, whatever the treatment. We cannot

achieve the impossible, and if we make the attempt and fail it cannot fairly be laid at the door of tuberculin. For these and other reasons I hold that statistical information is too full of fallacies to be really useful, but I would refer those who are interested in this part of the subject to Dr. Lawrason Brown's article in Kleb's volume on "Tuberculosis."

Another method—also open to many fallacies—of estimating the value of tuberculin is the *a priori* method. For example, we have now accumulated a good deal of information concerning the value of vaccine therapy in a number of other diseases, and although this method has its limitations, I think we shall be all agreed in holding that vaccine therapy is a great addition to our therapeutical resources. We would by analogy expect tuberculin to be of value. Again, during recent years we have been able, as the result of the work of Sir Almroth Wright and, especially in this connexion, of Dr. Inman, to formulate a working hypothesis which makes a strong appeal to many of us, as an explanation of the effects of sanatorium treatment. I refer to the theory of auto-inoculation. It would seem to be proved that movement or exercise determines to some extent the amount of lymph and blood which passes through a diseased lung in a given time, and that this in turn determines the amount of bacterial products absorbed into the general circulation, and so determines the task set the defensive forces of the body. This theory is not the whole story, it takes no account of the action of ferments, the products of the destruction of tissue, and other possible factors, but it would seem to show that we can to some extent limit or increase the absorption of bacterial products by rest and exercise. The bacterial products are in the main the patient's own tuberculin, that is to say, we are dealing with "autogenous inoculation" in sanatorium treatment. In support of this I would mention that the effect of exercise in this treatment, and the effect of a hypodermic or oral dose of tuberculin, is precisely similar. Over-exertion, or an overdose of tuberculin administered hypodermically or orally, produces precisely the same clinical symptoms—malaise, headache, increase of expectoration, fever, &c.; whereas a beneficial amount of exercise or a suitable dose of tuberculin produce strictly comparable clinical effects. I think we are all agreed that sanatorium treatment, properly carried out, in suitable cases gives good results and that in the main this depends chiefly upon the proper regulation of exertion. If this is so, we have a good *a priori* argument as to the value of tuberculin.

All these methods of estimating the value of tuberculin are

unsatisfactory. We have, therefore, to rely upon the impressions formed by clinical observers. There are fallacies in this as in other methods, but it is the method upon which many of our advances in therapeutical knowledge have been obtained. A discussion such as this should help us to form conclusions. I think we shall find that those who have much experience are convinced of the value of tuberculin in pulmonary tuberculosis as in other forms of the disease, and that opposition comes almost wholly from those whose experience of the remedy as now given is limited or one of hearsay. That tuberculin in this connexion is of value is accepted in Germany and in America. It is also a significant fact that whereas six years ago tuberculin was not used in more than two or three institutions in this country it is now stated to be employed as a routine measure in over two hundred.

PREPARATIONS OF TUBERCULIN.

One of the difficulties of tuberculin treatment is the number of different preparations. For the convenience of the Section I give below a table of some of the chief varieties and their method of manufacture. It is evident from this table that at present we lack anything like efficient standardization of the different preparations, and consequently the same dose of preparations with the same name have at times different effects on the same patient. I would draw attention also to the fact that the age of the preparation and the length of time a solution has been in existence must be taken into account. It is not an uncommon thing to find that when a fresh solution is employed the effect of a particular dose is more marked than the effect of the same dose of a month-old solution, and sometimes in this way undesirable reactions are produced. My experience suggests that it is important to employ solutions which have been recently prepared. Again there is difficulty in comparing the toxicity of the different preparations, or in saying how much of one may be regarded as equivalent to a certain dose of another. Another point which this list brings out is the fact that there is a marked and essential difference between the various preparations. For example, old tuberculin consists of exotoxins and a certain amount of endotoxins. Tuberculin T.R. consists of endotoxins only, and T.O.A. or P.T.O. consists of exotoxins only, whereas B.E. may be regarded as a true vaccine. Different observers pin their faith to different preparations, and the astonishing thing is that the results of all appear to be the same in spite of the fact that there are such essential differences in the tuberculin used. This emphasizes the fact that our

knowledge of the subject is by no means final. The custom of many authorities of giving a course of P.T.O., then a course of P.T., and finally a course of old tuberculin has a good deal to recommend it in view of the above, but I would say that I see no special virtue in bovine preparations and that I am not convinced, by the evidence hitherto brought forward, that it is preferable to use bovine preparations in pulmonary tuberculosis and human preparations in so-called surgical tuberculosis. My own experience has been mainly with T.R. or B.E. and to a less extent with P.T.O., and subsequently P.T. and old tuberculin. T.R. is, I think, especially useful in febrile cases. B.E. is the cheapest preparation, and is probably the most widely used form. It has the objection that it is more prone than most to cause painful local infiltrations. To overcome this we have the S.B.E., but our experience of this form is not yet sufficiently large to allow any useful deduction to be made. In some cases tuberculin has been prepared from the patient's own strain, and on the analogy of vaccine therapy generally it is possible that an autogenous B.E. might be the best thing to use.

There are a certain number of patients who have peculiar idiosyncrasies for one or other preparation, being more sensitive, it may be, to T.R. or B.E. or P.T.O. Whenever there is evidence of undue sensibility to any given preparation it is best to try the effect of another.

THE TUBERCULINS.¹

HUMAN.

(1) OLD TUBERCULIN (*Tuberculinum Kochi*).

Preparation.—OLD TUBERCULIN is prepared from a four to five weeks' old culture of tubercle bacilli of a human strain, by evaporating to one-tenth of its bulk, at a temperature not exceeding 70° C., and filtering through suitable filters. It consists of exotoxins and a certain amount of endotoxins obtained in the process of evaporation.

Employment.—For diagnosis and treatment.

(2) TUBERCULIN T.R. (*Koch's New Tuberculin*).

Preparation.—Triturated tubercle bacilli of a human strain are centrifugalized with sterilized water until all soluble products are dissolved. The supernatant liquid containing water-soluble toxins (termed T.O. by Koch) is rejected. By alternately treating the insoluble bacterial matter with sterilized water and centrifugalizing a number of exceedingly fine emulsions are obtained, which on being bulked represent T.R.

1 c.c. T.R. contains the active—i.e., the insoluble—bacterial matter of 10 mg. of tubercle bacilli. A number of tests have shown this to represent 2 mg. of solid substance.

Employment.—For treatment only.

BOVINE.

(1) BOVINE TUBERCULIN (*P.T. from the German Perlsucht Tuberculin*).

Note.—All bovine tuberculins in this column are prepared in an analogous manner to the corresponding tuberculins in the "HUMAN" column—the sole difference being that tubercle bacilli of a bovine strain are employed.

Employment.—For diagnosis and treatment.

(2) BOVINE TUBERCULIN T.R. (*Tuberculin P.T.R.*).

Preparation.—See Note above.

Employment.—For treatment only.

¹ A Table drawn up for the purpose of this article by Meister, Lucius and Brüning, Ltd., 3, Jewry Street, London, E.C.

THE TUBERCULINS—(continued).

HUMAN.

(3) NEW TUBERCULIN BACILLI EMULSION
(*Tuberculin B.E.*).

Preparation.—0.5 gm. of triturated human tubercle bacilli is emulsified with a mixture of 50 c.c. glycerine and 50 c.c. sterilized water.

1 c.c. B.E. contains 5 mg. bacillary substance.

Employment.—For treatment only.

(4) T.O.A.

Preparation.—Four to five weeks' old cultures of human tubercle bacilli are filtered through bacteria filters. The absolutely germ-free filtrate constitutes T.O.A.

It consists of exotoxins solely.

Employment.—For treatment only.

(5) VACUUM TUBERCULIN.

Preparation.—T.O.A. evaporated to one-tenth its bulk at a low temperature and in partial vacuum.

Employment.—For treatment only.

(6) TUBERCULIN A.F. (*Koch's albumose-free Tuberculin*).

Preparation.—TUBERCULIN A.F. is prepared from tubercle bacilli of a human strain which have been cultivated in a special medium consisting of inorganic salts and citrates, the sole nitrogenous constituent being asparagin. All additions of albumoses, peptone and extractive matters from flesh and blood are avoided.

Employment.—The mode of employment conforms in all particulars with that of OLD TUBERCULIN, with which it corresponds in respect of its active value.

The advantage of A.F. over OLD TUBERCULIN consists in the strictly specific character of the reactions induced by it, and that anaphylactic symptoms are excluded in consequence of the absence of non-specific proteins.

(7) TUBERCULOSIS SERO-VACCINE.

EMULSION OF SENSITIZED TUBERCLE BACILLI
(S.B.E.).

Preparation.—Well washed and sharply dried tubercle bacilli of a human strain are mixed with a quantity of fresh tuberculosis serum and kept several days in the incubator at 37° C., and then worked in a shaking apparatus with glass beads until no whole tubercle bacilli can be detected in a sample of the same. The disintegrated bacillary masses are then separated from the serum by centrifugalization, washed with physiological saline solution and finally made into a fine emulsion with 40 per cent. glycerine water, to which 0.5 per cent. carbolic acid has been added.

1 c.c. S.B.E. contains 5 mg. bacillary substance.

Employment.—For treatment only.

BOVINE.

(3) BOVINE TUBERCLE BACILLI EMULSION (*Tuberculin P.B.E.*).

Preparation.—See note above.

Employment.—For treatment only.

(4) P.T.O.

Preparation.—See note above.

Employment.—For treatment only.

(5) BOVINE VACUUM TUBERCULIN.

Preparation.—P.T.O. evaporated to one-tenth its bulk at a low temperature and in partial vacuum.

Employment.—For treatment only.

By special request a Bovine S.B.F.
is supplied by the makers.

CLASS OF CASE FOR TUBERCULIN THERAPY.

Although I would by no means go so far as some authorities who hold that tuberculin should not be given whenever there is evidence of secondary infection, I cannot emphasize too strongly the necessity for care in the selection of cases for this treatment. There can be no doubt that tuberculin is capable of doing a great deal of harm, not only when improper dosage is employed but also in comparatively large groups of cases. At one time I was not infrequently asked to demonstrate the value of tuberculin in cases which were obviously hopeless. To expect tuberculin to produce a miracle is foolish, and any expectation of good from a course of tuberculin in a series of advanced febrile cases in which there is marked secondary infection is foredoomed to disappointment. My experience suggests that tuberculin will not only do no good, but will cause harmful results in those cases in which there is more or less constant auto-inoculation, for example, cases in which frequent attacks of prolonged coughing or other symptoms produce a series of auto-inoculations which are beyond our control. If we give tuberculin in such a case we increase what may already be an excessive dose of the patient's own bacterial products, and so merely court disaster. We must not, however, generalize too freely, for every case has to be considered on its individual merits. In spite of this we may say that the ideal cases for tuberculin therapy are the cases of recent origin with little constitutional disturbance and chronic afebrile cases, that is the cases in which walking exercise to the extent of a few miles produces no febrile reaction. Another class of case in which tuberculin is of great value, in that it may enable the patient to "turn the corner," is the class of case in which there is no real progress in spite of more or less prolonged treatment on sanatorium lines, but in which the patient is just holding his own. These, of course, are the classes in which the majority of observers have obtained the best results. I think, however, that tuberculin has not been given sufficiently in febrile pulmonary tuberculosis, although its use in such cases is much more difficult and calls for mature experience and judgment. In those cases in which there is much irregularity with regard to the rises of temperature, and in which all our efforts fail to control this symptom, tuberculin does harm. It is, however, possible sometimes to control the cause of these irregular auto-inoculations. For example, a harassing cough involving much movement and fatigue may sometimes be controlled by the use of sedatives, such as codeine or the continuous

inhalations of antiseptic remedies; active laryngeal tuberculosis may be controlled by vocal rest, or frequent vomiting may be relieved by appropriate remedies. Or, again, it is possible in a certain number of cases to control the auto-inoculations by means of what is called by the unfortunate name of artificial pneumothorax or compression of the diseased lung by means of nitrogen. When we can control the amount of auto-inoculation in this way and also in cases of febrile disease in which the auto-inoculations are more or less regular, my belief is that tuberculin may often greatly improve the chances of recovery, and I would urge its wider use in such instances at the hands of experts. One further point under this heading. In all forms of tuberculosis in which there is definite caseation and breaking down of the tissues, tuberculin will accentuate the intoxication if there is no outlet to the necrosed products, and similarly in pulmonary tuberculosis with marked and active caseation, the use of tuberculin accentuates the activity of the process. In some cases this is of value, as it leads to rapid breaking down of a localized area with cavity formation and subsequent healing.

DOSAGE AND SPACING OF DOSES.

In the choice of the initial dose and in the subsequent increase of dose the greatest care is required, and due consideration must be given to the peculiarities of each individual case. There is no need to hurry, for tuberculin treatment is a matter of months and not weeks. It will be found that in nearly every case, sooner or later, there is a period of difficulty owing to the sensibility of the patient to the remedy. Once this is over rapid progress, as a rule, occurs and increase of dosage is comparatively easy. In a smaller proportion of cases there is, however, constant difficulty owing to the sensibility of the patient, and in these it is a good plan to repeat the same dose for a considerable time and to refrain from frequent increases. We may now discuss the question of dosage under two broad headings: (1) Chronic afebrile cases; (2) febrile cases.

(1) Chronic Afebrile Cases.

The Initial Dose.—This naturally depends on the preparation used. There is a wide difference in the size of the initial dose employed by different authorities. In many cases it is possible to commence with a comparatively large dose (such as $\frac{1}{20000}$ mg. or 0.000005 c.c. T.R.) and to increase the size of the dose rapidly (*see* Chart 1). In a small

Subsequent Doses.—In this connexion there are two schools: those who believe in producing a general reaction or see no objection in doing so, and those who hold that a general reaction may do so much harm that it should be avoided when this is possible. There is no question that in many chronic cases a general reaction, even when accompanied by considerable fever, which does not last more than twenty-four hours, is followed by very considerable improvement all round. In such an event, if we wait and then repeat the same dose, we will usually cause a

further reaction, but a less severe one. If we wait further and then repeat the same dose again, there may be no reaction, and the patient is, so to speak, over the stile (*see* Charts 2 and 3). We may safely increase the dose until a further reaction is produced. When this occurs we go through the same procedure. In a certain number of instances, however, and especially in those cases in which there is a more or less ready tendency to auto-inoculation, the reaction caused

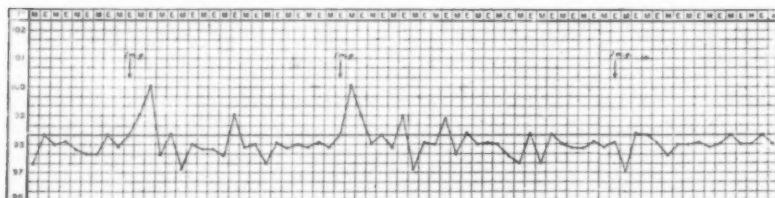


CHART 2.

The effect of tuberculin (1 mg. injected subcutaneously) in a case of afebrile chronic pulmonary tuberculosis (two lobes and excavation; tubercle bacilli present in the sputum). It will be noticed that the first dose caused a temporary rise of temperature to 100° F.; the second dose caused a temporary rise of temperature to 100° F.; whilst the third dose produced no rise, but a flattening of the temperature.

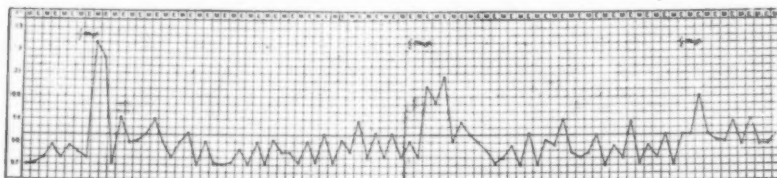


CHART 3.

The effect of tuberculin ($\frac{1}{2}$ mg.) injected subcutaneously in a case of afebrile chronic pulmonary tuberculosis (two lobes and excavation; tubercle bacilli present in the sputum). It will be noticed that the first dose caused a temporary rise of temperature to 102° F.; the second dose caused a temporary rise of temperature to 100.8° F.; whilst the third dose caused a temporary rise to 100° F.

may last for days and even for weeks. When this happens the sensibility of the patient to tuberculin is sometimes much enhanced, and tuberculin treatment becomes more difficult or even impossible. As we have no real guide to the class of case in which a prolonged general reaction is likely to occur, it is best to avoid its production

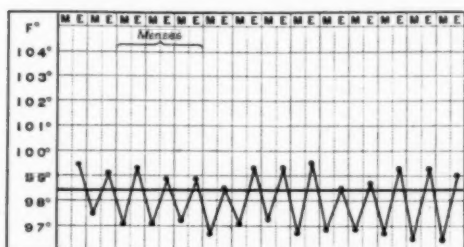


CHART 4.

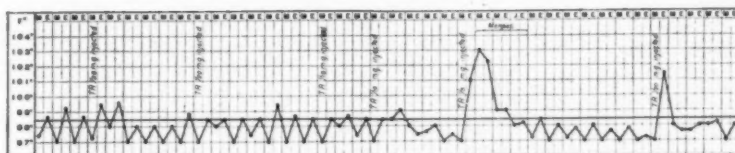


CHART 4A.

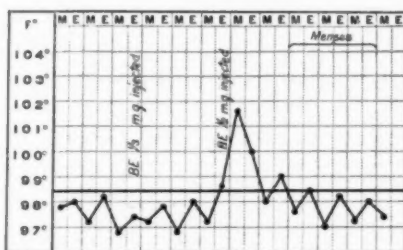


CHART 4B.

Girl, aged 17. Four years' history. Infiltration throughout right lung, and to a considerable extent in upper left lobe. Tubercle bacilli present. The first chart shows the type of temperature on admission. The second chart shows (a) improvement of temperature, e.g., after $\frac{1}{10}$ mg. T.R.; (b) practically no reaction after $\frac{1}{10}$ mg.; (c) small reaction after $\frac{1}{10}$ mg.; (d) big reaction after $\frac{1}{10}$ mg., which was probably due to the fact that this dose was injected just before the commencement of menstruation; (e) marked improvement of the temperature after this reaction; (f) sharp reaction after $\frac{1}{10}$ mg., although this dose when given previously caused no reaction. The third chart shows no reaction after $\frac{1}{10}$ mg. B.E. (which was substituted for T.R. on account of expense), but a reaction after $\frac{1}{10}$ mg. B.E. which again was probably connected with menstruation. In this case at first there was amenorrhoea. Menstruation is now rather too frequent. There has been a gain in weight of 14 lb. in four months. No tubercle bacilli have been found in the last six examinations.

as far as possible. This may mean some delay, but in tuberculin therapy time is comparatively unimportant, and in any case delay is better than possible disaster. A general reaction can usually be avoided by careful observation of the clinical symptoms, as these will give us warning that the dosage is becoming excessive before a general reaction is produced. *An excessive dose* will produce malaise, headache across the eyes, excessive focal reaction, as is evidenced by an undue increase of crepitations over the diseased area and an undue increase of expectoration, and a definite effect on the temperature. Such a dose will either increase the size of the daily excursions of the temperature (whether normal, subnormal, or above normal), or produce a rise of temperature. A particular dose may have this effect more readily at certain times. For example, it is well known that in many consumptive women there is a rise of temperature for, it may be, as long as fourteen days before menstruation, which abates as soon as the flow is established. As a rule this rise of temperature may be disregarded, but in some instances a dose of tuberculin when given during this time will be excessive, whereas at other times it produces no reaction (*see* Charts 4, 4A, 4B). Similarly, we must bear in mind that a dose may produce excessive reaction unless care is taken to limit the amount of auto-inoculation produced on the day on which the dose is given. For this reason it is wise to prescribe rest or merely gentle exercise on the day on which the dose is given. In my experience a general reaction, even in those cases in which it is followed by beneficial results, does nothing which cannot be obtained by doses which fall short of producing it, whereas a general reaction may be prolonged and cause irremediable mischief. To me, therefore, it seems obvious that we should endeavour to avoid a general reaction, by avoiding any increase of dose whenever we have evidence—which we usually can obtain by a sufficiently close clinical observation—that we are on the borderline. If we do produce a general reaction, in my opinion it is a wiser policy not to repeat the same dose when the reaction is over, but to mark time with a rather smaller one.

Apart from this it is necessary for the purpose of spacing doses to know what is an ineffective dose and what is an effective dose. *An ineffective dose* produces no focal reaction, and has no effect upon the temperature, and consequently the next dose may be safely increased in size and given at a short interval. *An effective dose* produces a focal reaction, and so a temporary increase of expectoration, and may cause a lowering of the temperature or a diminution of the daily excursions and so

"flattening" of the temperature (whether subnormal, normal, or above the normal). An effective dose may sometimes be repeated with advantage, but as a rule—and here experience alone helps us—the next dose should be a larger one, and may be given at two to three day intervals, when the dose is small, or at five to ten day intervals as the dose becomes larger.

The Final Dose.—Here, again, we have two schools—those who hold that we should aim at large doses such as 20 mg. or more of B.E., or 1 c.c. of O.T., and those who are satisfied with such a dose as $\frac{1}{10000}$ mg. (0.00002 c.c.) B.E. My own view is that we should aim at the larger doses. This is not always possible of attainment, for in a number of cases a particular dose, such, for example, as $\frac{1}{100}$ mg. (0.002 c.c.) B.E., will always produce a general reaction and it is impossible to increase the dose. Fortunately the results in these cases are often satisfactory.

(2) In Febrile Cases.

In these cases tuberculin therapy is still more difficult and calls for even greater care. The principles of treatment are the same, except that we must use every measure at our hand to prevent auto-inoculation. Here, certainly, we should avoid any general reaction. The initial dose should not exceed $\frac{1}{500000}$ mg. (0.0000004 c.c.) B.E., or (0.0000002 c.c.) T.R., and the increase of dosage must be very gradual. In certain cases benefit follows the repeated administration of the same dose without any increase for a time. Any dose of such a size can only have a transitory effect, and it is therefore necessary that the intervals between the doses should be small, as a rule forty-eight to seventy-two hours. I give below three charts, one from a case of generalized tuberculosis and two from cases of acute febrile pulmonary tuberculosis to show that even here tuberculin may be of great service (see Charts 5, 6 and 7).

METHOD OF ADMINISTRATION.

The usual and most satisfactory method of administration is by means of hypodermic injection, and it may be as well to state that it is advisable to utilize different sites for the various doses. Some years back I brought forward, in conjunction with Dr. Spitta and Dr. Inman,¹ evidence to show that it was possible to administer tuberculin T.R. by the mouth under certain conditions, of which I gave precise details, and

¹ *Proceedings*, 1908, i (Med. Sect.), pp. 195-252.

I have had the satisfaction of having my observations confirmed by a number of other workers. I have been subjected to much criticism in this direction, but much of this criticism is due—as so often happens in medical questions—to the fact that views have been attributed to me which I have not expressed. I brought forward the question of oral administration, not as an improvement on hypodermic administration, but as a possible alternative when circumstances made the hypodermic

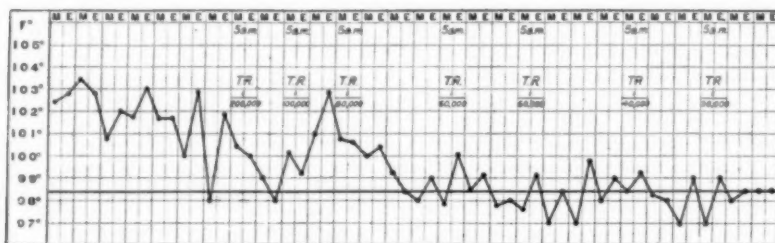


CHART 5.

Woman, aged 20. Two years' history of illness; infiltration throughout right lung, and in apex of left lung. The temperature in this case was the same as, or higher than, in the first twelve days of the chart. The chart shows the effect of the oral administration of Burroughs Wellcome & Co.'s tuberculin W. The temperature continued to be satisfactory.

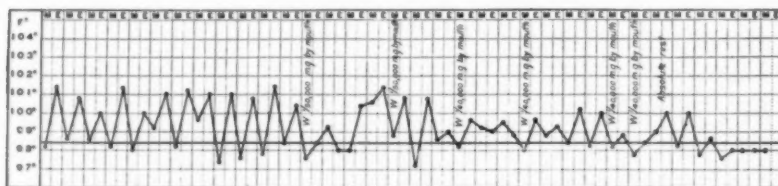
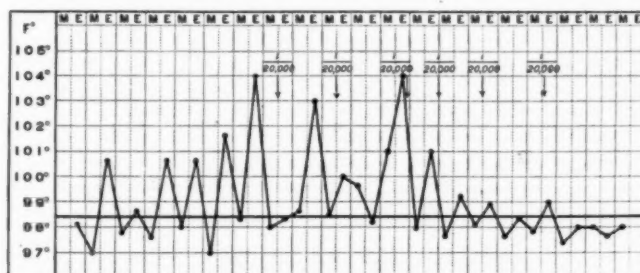


CHART 6.

Man, aged 26. First seen after a month's history. Acute caseous tuberculosis in upper lobes on both sides. Tubercle bacilli present. Absolute rest for a week produced little effect. The administration of tuberculin by the mouth was followed rapidly by a cessation of fever, and it is possible here to see the effect of each dose given. In a month's time the temperature became normal. The patient was subsequently sent to a sanatorium, and is now at work.

method difficult or impossible. I am told, what appears to be true, that old tuberculin is not absorbed by the stomach. I never said it was. I confined my observations to T.R. Old tuberculin contains chiefly exotoxins and T.R. endotoxins, and the preparations are not, therefore,

strictly comparable. Again, many of those who contest the absorption of T.R. by the stomach have been at no pains to give the dose in a fluid isotonic with the blood on an empty stomach and without the addition of antiseptics. I emphasized the importance of an empty stomach, and failure to obtain absorption when the dose is given under other conditions is no criticism on my observations. Tuberculin given in this way cannot stimulate the secretion of gastric juice, and the question of digestion does not arise, especially as the chief function of the stomach is absorption. It is quite true that in some individuals absorption by the stomach is unsatisfactory. This I pointed out when I said that absorption could not be anticipated when the stomach was disordered or the



same clinical symptoms (see Charts 8 and 9). An overdose will give a general reaction, an effective dose will give a focal reaction. Absorption by the stomach is not a variable thing, for I have found that a particular dose, say, $\frac{1}{300000}$ mg. T.R., given in this manner produces good results, whereas so small an increase as $\frac{1}{250000}$ mg. may produce in certain cases a general reaction. I have seen prolonged reactions in acute cases as the result of the oral administration of $\frac{1}{1000000}$ mg. T.R. A dose of any vaccine, however administered, which is followed by a focal reaction must convince any bacteriologist, or anyone with a

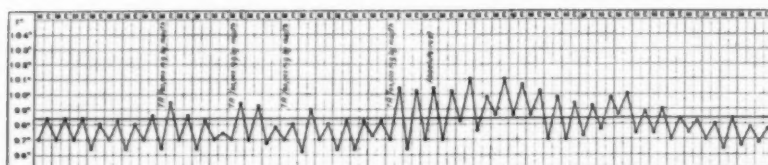


CHART 8.

Man, aged 19. Six months' history of tuberculous pleurisy. This chart shows the result of oral administration in a susceptible case. Tuberculin was continued in this case with good results.

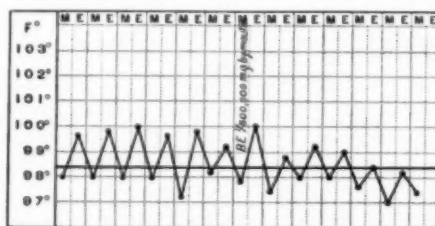


CHART 9.

Woman, aged 22. Eighteen months' history. Infiltration throughout right lung, and to a slight extent in apex of left lung. Tubercle bacilli present. Under observation without improvement at Northwood Sanatorium for six months. The chart shows the apparent effect of the oral administration of a minute dose of B.E. Subsequently an artificial pneumothorax was induced, and the patient at the present time is having nitrogen injections and tuberculin.

knowledge of vaccine therapy, that absorption has taken place, and I would ask those who do not believe in the absorption of T.R., without antiseptic additions and on an empty stomach, to repeat my observations and watch for focal reactions, for they will certainly find them. For example, doses given in this manner will produce a reddening of the

larynx in laryngeal tuberculosis, and will increase the moist sounds in the diseased area in pulmonary tuberculosis, and will give evidence of focal reaction in other forms of the disease.

I find that it is possible to obtain a marked degree of immunity to tuberculin by oral administration even in cases of advanced disease. It is possible (*see* Charts 10 and 11) to give tuberculin by the mouth until

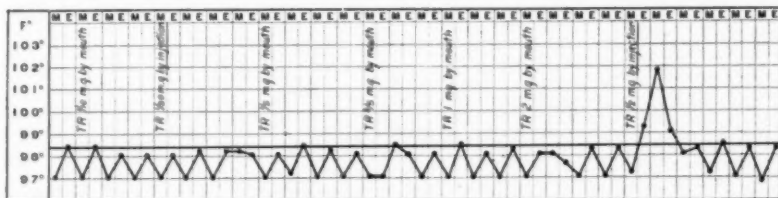


CHART 10.

Man, aged 39. Two and a half years' history. Infiltration apex of right upper and lower lobes and in left upper apex. Tubercle bacilli present. This chart shows (a) a dose of $\frac{1}{10}$ mg. T.R., by hypodermic injection, after a dose of $\frac{1}{10}$ mg. T.R. has been reached by oral administration, produces no reaction; (b) a dose of $\frac{1}{10}$ mg. T.R. by injection, after a dose of 2 mg. T.R. by mouth had been given without reaction, caused a severe but temporary general reaction with marked malaise.

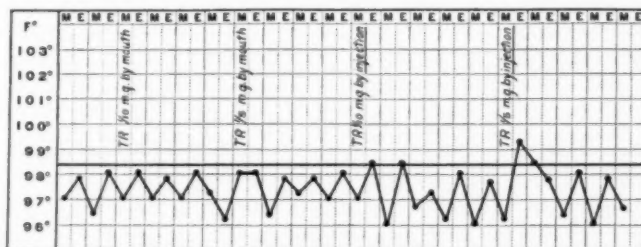


CHART 11.

Man, aged 35. Nine months' history. Infiltration throughout left lung and in right upper lobe. Tubercle bacilli present. This chart shows that there was little reaction when a dose ($\frac{1}{10}$ mg. T.R.) was given for the first time by the hypodermic method after a dose of $\frac{1}{10}$ mg. had been reached by the oral method.

a dose of $\frac{1}{30}$ mg. T.R. is reached, and then to give a hypodermic dose for the first time of as much as $\frac{1}{10}$ mg., without producing a reaction. In cases of advanced disease an initial hypodermic dose of $\frac{1}{10}$ mg. T.R. would certainly produce a reaction: the fact that it does not when tuberculin has been administered orally for some time affords definite

proof that a degree of immunity has been established. These charts show, however, that there is a limit to the capacity of the stomach for absorption of this remedy. If I give T.R. by the mouth until a dose of 1 mg. is reached, and then give $\frac{1}{2}$ mg. as the first hypodermic dose, I always produce a general reaction. In such cases the temperature rises to 101° F. or 102° F., but the reaction is over in twenty-four hours. An initial hypodermic dose of $\frac{1}{2}$ mg. in cases with extensive disease would produce disaster, and the fact that it only produces a temporary reaction appears to me to prove the efficacy of oral administration.

Our knowledge of immunity is so small that it is unwise to condemn any method without adequate examination, and I would suggest to my critics that the natural immunity we all possess is not produced through absorption of bacteria or their products by the skin, but through absorption from the alimentary canal, and that it is possible that absorption through the alimentary canal may play a sufficiently large part in the question of immunity to make it worthy of further investigation.

DURATION OF TREATMENT.

Treatment in all cases should be prolonged. Even in those cases in which there has never been any marked constitutional disturbance the duration of treatment should not be less than eight months, and may preferably be put at one year. Each case, in this respect as in others, must be treated on its merits and it is impossible to lay down stringent rules. This applies especially to cases in which there has been more or less marked constitutional disturbance and a more or less ready tendency to auto-inoculation. In such the duration of treatment may be eighteen months or even more. By tuberculin we raise the immunizing capacity, and our aim is to raise it to the highest point possible for the individual case; we must therefore continue it for some little time after we have arrived at the stage in which even considerable exertion fails to produce any evidence of auto-inoculation. In a number of cases two or more courses of tuberculin may be necessary at an interval of a few months.

NECESSITY FOR COMBINING TUBERCULIN THERAPY WITH OTHER MEASURES.

It is hardly necessary to insist that tuberculin is but one factor in the treatment of pulmonary tuberculosis, and I would not allude to this point if there were not some danger at the present time of too much

attention being focused on this remedy, to the exclusion of all other methods of treatment. In the fight against the invasion of tubercle bacilli into the human body we rely on measures which increase the capacity of our complex defensive forces, or capacity for adequate immunizing responses or which diminish the call on these forces. Consequently the regulation of exertion, the provision of healthy surroundings, and a constant supply of fresh air and adequate nourishment, each have their place. The treatment of this disease must be regarded sanely and as a whole, and in my opinion is best carried out in the greater number of cases in an institution, as this allows for the most important factor of all, namely, constant medical supervision. Those who preach that tuberculin is the only thing of real importance are doing much to limit the good effects of the present campaign against tuberculosis, not only in its curative aspect, but from the preventive side as well.

THE USE OF TUBERCULIN WHEN SECONDARY INFECTION IS PRESENT.

The part played by secondary infection in pulmonary tuberculosis requires much closer consideration than it has hitherto received. Our knowledge on the subject is fragmentary. So far as my experience has gone, I would say that when the tuberculous infection is the dominant factor there is no reason why tuberculin should not be used with success. It may be of service to attack the secondary organisms simultaneously by means of appropriate vaccines. In many cases, especially those in the later stages of the disease, the dominant factor appears to be the secondary infection rather than the tubercle bacillus. In such cases the use of tuberculin is often disappointing, and in certain instances I think—although I can give no explanation—that after the use of tuberculin there is increased activity of the secondary infection, and to a less extent there is increased activity of the tuberculous process after the use of a secondary vaccine.

In connexion with the question of secondary infection, I would mention that I have seen a certain number of cases of what have been regarded as examples of chronic pulmonary tuberculosis (with to my own knowledge an undoubted history of former tubercle), in which tubercle bacilli have been absent from the sputum for long periods, and in which all the symptoms have been due to secondary organisms. In these cases vaccine therapy often improves the general condition and comfort of the patient to a surprising degree.

CONCLUSIONS.

My experience of the last six years, which included several hundred cases, has led me to form the impression that the *careful* use of tuberculin gives valuable results in the treatment of pulmonary tuberculosis. Its use is not attended with dramatic effect except in occasional examples of febrile disease or laryngeal tuberculosis, nor does its use tend to hasten the apparent arrest of the disease or shorten the length of treatment required, except in certain instances in which the patient is just holding his own but is making no real progress. On the other hand, tuberculin, in conjunction with ordinary methods, will lead to the disappearance of tubercle bacilli from the sputum in a larger proportion of cases than ordinary methods alone, and in my experience diminishes the number of relapses, or, in other words, establishes a higher degree of immunity. In view of these facts, I agree with those who hold that the best treatment for pulmonary tuberculosis is tuberculin treatment in conjunction with what is called sanatorium treatment, either at a special institution—as is necessary in a considerable proportion of cases—or at home.

DISCUSSION.

Dr. NATHAN RAW: The treatment of tuberculosis is of such intense urgency and importance that we are compelled thoroughly to test any method which is based on scientific investigation and experience, with a view to reducing the awful amount of pain and suffering produced by this disease. After a large experience in the treatment of tuberculosis in all its forms I have come to the firm conclusion that tuberculin is a valuable remedy in a large number of cases. In the treatment of all disease we would naturally expect to get the best results in mild or early cases, and this rule applies with special force in dealing with tuberculosis. It must not be assumed, however, that advanced cases are not benefited, for I have repeatedly seen patients with long-standing pulmonary tuberculosis greatly improved by continuous injections of tuberculin.

During the last fifteen years I have treated 400 cases of tuberculosis with tuberculin, and after a careful study of the hospital and other notes, I have come to the conclusion that it would be of no value or assistance to enumerate the results of treatment, for the simple reason

that so many of the patients cannot be traced after leaving hospital and sanatorium. The fact, however, remains, that a large number of patients are alive and well to-day who were treated with tuberculin six years ago, and who I feel certain would not have lived otherwise.

It cannot, however, be too strongly emphasized that tuberculin is a powerful drug, which ought only to be used on the advice of a specialist in the treatment of tuberculosis, and that great care and supervision are absolutely essential in its administration. I will never forget giving my first injection of tuberculin twenty-one years ago to a young man, the subject of severe lupus of the face. The tuberculin was received direct from Berlin, and the stated amount was injected between the shoulder-blades. In the course of a few hours the patient had a violent rigor and his temperature rose to 105° F., with a bounding pulse of 140. There was a terrific reaction in the lupoid area, the patient vomited continuously, and he said he was dying. The site of injection was acutely inflamed, and the skin over the face, neck and chest was of a scarlet hue. This state of things continued for four days, when the symptoms gradually subsided and he recovered, quite contrary to our expectations. There was, however, great improvement in the state of the lupus, which from being a large, disfiguring ulcer became cicatrized and soundly healed, only to break down again in a few months. I received such a fright, that I did not use tuberculin again until 1897, when Koch introduced his tuberculin T.R., or what was called new tuberculin.

The whole fault of Koch's original tuberculin was in the dosage, which was excessive, and I venture to think that we now understand not only the doses required for each particular case, but also the exact procedure for its administration. We must always expect to obtain better results in localized deposits of tubercle, such as glands, joints and lupus, than in a more general infection of the lungs. I am an ardent follower of the teaching of our great master, Koch, who first established the duality of tuberculosis. Two distinct types of bacilli must be recognized: (1) *typus humanus*; (2) *typus bovinus*. Bacilli of the *typus humanus* probably produce consumption, tuberculous laryngitis and secondary intestinal ulceration with fistula in ano, whilst bacilli of the *typus bovinus* produce abdominal tuberculosis, acute urinary tuberculosis, tuberculosis of bones and joints, enlarged glands, meningitis, and probably lupus. These types are entirely different and antagonistic to each other, so that a person who has been attacked by consumption, which is a human infection, is not likely to develop tuberculosis of the joints or glands, and conversely a child who has suffered from tuberculous spine or

joints is not likely to develop phthisis pulmonalis. In fact one infection protects against the other, and the toxins or vaccines are reciprocal, and act as vaccines to each other. It is necessary for me to make this quite clear so as to explain my reason for using a tuberculin prepared from bovine bacilli in the treatment of pulmonary tuberculosis or consumption.

In the treatment of a human infection we should use the opposite tuberculin, viz., bovine, and in the treatment of a bovine infection such as of glands, bones and joints we should use a tuberculin prepared from human bacilli such as Koch's old tuberculin, much in the same way as vaccinia being a modified form of small-pox is used to protect against small-pox itself. I have found, moreover, that bovine tuberculin is much less toxic than a human preparation, and is less likely to produce reactions. Bovine tuberculin is, however, only used by me in the treatment of pulmonary tuberculosis, and I invariably treat the so-called surgical or local manifestations of tuberculosis with human tuberculin.

During the last fifteen years, out of over 6,000 cases of tuberculosis with which I have had to deal, I have only used tuberculin in 408. This small percentage is explained by the fact that up to six years ago I was somewhat sceptical of the value of the drug in pulmonary tuberculosis, whereas now I am convinced of its value; and also, that a large number of my cases are sent into hospital in such an advanced stage of the disease that no treatment is of any avail in avoiding a fatal termination. My tuberculin cases were as follows:—

Pulmonary tuberculosis	198	with bovine tuberculin
Glandular	"	107	" human "
Abdominal	"	47	" "
Lupus	"	32	" "
Joints and bones	41	" "
Genito-urinary	36	" "
Meningitis	7	" "
					408	

The length of treatment was never less than three months, and in many cases it extended for over twelve or even eighteen months. The conditions with regard to fresh air and climate were most unfavourable, as the majority were treated in the centre of Liverpool in a crowded atmosphere, notwithstanding which, in my opinion, the results have been satisfactory, and in many cases remarkable. I am most anxious not to overstate the case with regard to results, but in spite of the fact that I have lost trace of a great number of the patients during the last ten years, I think I am safe in saying that 55 to 60 per cent. of the cases of pulmonary tuberculosis are living now, many of them to my knowledge

in excellent health. My best results have been obtained in tuberculous lymph glands, and I have come to look upon human tuberculin as a specific treatment. It is my invariable rule never to give tuberculin if there is any suppuration present or even threatened. In these cases the glands must either be aspirated or excised, as tuberculin has the effect of producing a violent local reaction with liberation of bacilli, and a possible blood-stream infection. When the pus is evacuated tuberculin is of great value. In a majority of cases treated the glands either disappeared altogether, or were greatly reduced in size. In seventeen excision was required, and in twenty-five cases aspiration or incision was necessary before the beneficial effects of tuberculin were obtained. In seven cases the glands extended direct to the pleura and apex of the lung, setting up a generalized pulmonary tuberculosis, all of which were fatal. Tuberculous peritonitis and mesenteric tuberculosis respond very quickly to tuberculin, and in several instances the disease seemed to be arrested altogether with tuberculin alone, but in thirteen of my cases it was necessary to open the abdomen and remove the fluid, which is evidently of a very toxic character.

With regard more particularly to the 138 pulmonary cases which were treated with tuberculin, 102 received bovine and thirty-six Koch's T.R. tuberculin. Of all the preparations of tuberculin which I have used I certainly prefer the bovine bacillary emulsion. It is prepared by using the entire body substance of the tubercle bacilli, and 1 c.c. of the emulsion contains 5 mg. of pulverized bovine bacilli. I have repeatedly had cases in which the bacilli disappeared from the sputum after twelve injections of bacillary emulsion.

Dosage.—Our object in administering tuberculin is to produce an active immunity in the body against the invading bacilli. In my opinion this immunity, to be lasting, must be very gradual, and if possible without local or general reactions. My procedure is as follows: The initial dose of 0.0001 mg. of bacillary emulsion is given with aseptic precautions, the patient being kept in bed for twelve hours before and twenty-four hours after to ensure complete rest and freedom from excitement. If nothing happens to contra-indicate, the dose is doubled in three days, and gradually raised to a maximum dose of $\frac{1}{10}$ mg. I have never given a larger dose, although some of my patients have received much larger doses on the Continent. The result is that I practically never see any signs of reaction, and the maximum dose may be repeated as often as is thought desirable, and in some cases it is advisable to give a course of tuberculin every six months for two or three years. The

contra-indications which I observe are: persistent temperature of 101° F.; hæmoptysis; severe mixed infection of lung and general debility, where the tissues make no effort at resistance, and the formation of antibodies.

In conclusion, I have not thought it desirable to lay statistics before you showing the results of treatment, for the reason that it is not possible even approximately to gauge the exact amount of good which has been done by any treatment in particular. Many of my patients have recovered without tuberculin, and I am glad to say a great many more have recovered with it, and I am convinced that the best treatment we have to offer to-day is the combination of sanatorium with tuberculin. I have injected forty children whose parents were phthisical with small doses of tuberculin, in the hope of establishing some degree of immunity and protecting them against a possible infection, but so far the results are negative, although I believe much may be done in that direction in the future. Tuberculin is a most valuable aid in the treatment of tuberculosis, but it must be used with care and discrimination, and with a full knowledge of its dosage and therapeutical effects.

DR. W. D'ESTE EMERY: I feel that an apology is due from me for taking part in this discussion, which I understand is to be on the use of tuberculin in phthisis. My experience in this disease has not been large, though I have seen and obtained good results in it. The cases I have treated have been mainly surgical, partly because I have had more opportunities in this direction, but mainly because I feel that in learning the use of a potent remedy like this, and one that is still in the experimental stage, it is best to begin with the simplest cases first. In cases of localized surgical tuberculosis, especially those of the iris and other parts of the eye, it is possible to follow every effect of the treatment, and to see at once whether it is doing good or harm. Further, it is easy to select cases in which secondary infections can be definitely excluded, and a potent cause of danger in tuberculin therapy thus avoided.

I should like to say a few words about the different kinds of tuberculin, since that is a source of difficulty to the beginner. There are two main classes of preparations, the soluble and the insoluble, corresponding to a very large extent to the exo- and the endo-toxins. The former consist of metabolic products given off by the bacilli, whilst the latter consist of substances which remain locked up in their protoplasm. Of the soluble tuberculins there are three forms, one unconcentrated, and consisting simply of the broth in which the bacilli

have been grown, one concentrated in the cold, and one concentrated at a temperature of about 70° C. Of the insoluble tuberculins there are two forms, one consisting of unaltered bacilli, and one consisting of bacilli in a fine state of subdivision. This gives us five forms of tuberculin, but there are really twice as many, since each is made from human and from bovine tubercle bacilli, and these preparations have different properties. Thus we have:—

(1) Unconcentrated tuberculin. This, if from human tubercle bacilli, is designated T.O.A., if from bovine bacilli P.T.O. (Perlsucht tuberculin original).

(2) Tuberculin concentrated in the cold, and called vacuum tuberculin and bovine vacuum tuberculin.

(3) Tuberculin concentrated at a raised temperature. This, if from human bacilli, is the familiar old tuberculin of Koch, the substance referred to when the term tuberculin is used without qualification. The corresponding bovine preparation is called bovine tuberculin, or more shortly P.T.

Of the insoluble forms we have:—

(1) The emulsion of bacilli, analogous to the ordinary vaccine. This is called *Bacillus emulsion* and *Bovine bacillus emulsion*, and referred to as B.E. and P.B.E. for the two forms respectively.

(2) The preparation of the finely ground bacilli, called T.R. and P.T.R. in the two forms.

Of these preparations I have had most experience of old tuberculin, *Bacillus emulsion*, T.R., and P.T.O. Of these preparations I am very strongly under the impression that the soluble forms are by far the most potent for good or ill. The substance to choose depends largely on the aim of your treatment: if you wish not to injure your patient and to do no harm, I think you will find T.R. the best form to use, whereas, if you wish to cure him, old tuberculin or P.T.O. will serve your turn best. As regards the difference between the human and the bovine forms, I think (though it is very difficult to make quite sure) that the bovine form, P.T.O., is milder and easier to handle, being less likely to cause violent reactions than the human form. I have not seen any evidence to make me think that human tuberculin is especially indicated in surgical tubercle, or in conditions due to the bovine bacillus, or vice versa. I have got very good results with both forms in surgical tubercle and in phthisis.

Here let me emphasize one point very strongly. Whatever form of tuberculin you use, it is absolutely necessary when you are dealing with

dilutions that these should be made up fresh. I have definite evidence that diluted tuberculin may become partially or entirely inert in a week or a little more: patients who have been thoroughly immunized to a certain dose of tuberculin not a fortnight old may give a violent reaction with half or three-quarters of the same dose of tuberculin taken from the same bottle, but just diluted. Where possible the dilutions should be made up twice a week, or once at the very least. If this is not done you may meet with violent reactions when passing from one dilution to another, and the course of treatment be fraught with danger.

May I also put in a plea for the system of recording the doses in terms of the amount of the remedy given, and not of the active ingredient it contains, or is supposed to contain? If you say you have given a patient $\frac{1}{100}$ c.c. of T.R. no one can possibly mistake your meaning, whereas there are two distinct systems of stating the amount of solid substance it is supposed to contain: an amount which you cannot possibly check.

Will you have patience with me whilst I give a brief outline of my own views of the method in which tuberculin acts? For some theory we must have, even though a faulty one; without it we shall learn nothing from our mistakes, and our methods will remain the merest guesswork. The theory I shall describe is, I believe, accurate as far as it goes, but there are certainly factors which have so far defied discovery.

I believe that practically everyone, certainly all adults in London, show some sign of possessing acquired immunity to tuberculosis. This is shown, amongst other ways, by the fact that almost all such persons have in their sera substances which possess the power of deviating complement in presence of tubercle bacilli, or of inhibiting such a combination when tubercle bacilli and antituberculous serum are incubated together. Excluding this latter phenomenon, which is not common and is at present unexplained, this indicates the presence of antibodies, which we know from other diseases are usually the accompaniments, if not the actual cause, of acquired immunity. Leaving out the cases which show the presence of this inhibiting substance, I find that complement disappears more or less rapidly when any serum, whether from a normal or from a tuberculous person, is mixed with tubercle bacilli, and I think it is fair to regard this as indicating the presence of antibodies, as in other diseases. Now in most tuberculous persons the amount of antibodies, as tested in this way, is greater than it is in health. In some cases it is enormously greater, and in quite general terms I find that the better the patient is

doing the greater the amount of antibodies. I may say at once that I do not believe it is possible as yet to estimate the degree of immunity which any person possesses to tuberculosis by the method of complement absorption, or by the opsonic index, or by any other process, but in the majority of cases the greater the amount of antibodies the better the prognosis. Now the first effect of tuberculin I shall discuss (it is not the first in point of time) is a notable increase in the amount of these antibodies, and I think we may fairly say, concurrently with this an increase in the degree of immunity to some at least of the tuberculous products formed in the body. A patient treated with tuberculin becomes less sensitive to the action of that substance, so that a larger amount has to be used to produce the same effect as was previously obtained with much smaller amounts. He is also less sensitive to auto-inoculation, and can take more exercise without a rise of temperature. If he has a purely tuberculous temperature to begin with, this often falls to normal: of course if it is due in part to a secondary infection to begin with this is not so easily accomplished. Tuberculin, then, in suitable doses can bring about at least a partial degree of immunity to tuberculosis. I say partial, for it is only too true that the disease may progress though the patient may appear, when tested by all the means at present at our disposal, to possess a degree of immunity much greater than normal.

Now to bring about this degree of immunity two conditions are necessary. The amounts of tuberculin given must be large, and the intervals between them suitable. If you give a long series of minute doses, such as are used by the supporters of the opsonic theory, the patient remains as susceptible as before, or may even become more so. This is because the doses are not large enough: as you will see subsequently, I do not say this method of treatment is useless, but I do say that it will not bring about any appreciable degree of immunity, unless, indeed, it is associated with graduated auto-inoculation, in which it is the latter procedure that is really efficacious in this respect. And the original method of giving tuberculin in rapidly increasing doses at short intervals, to the accompaniment of violent and often-repeated reactions, is also useless in this respect. The amounts given were large enough in all conscience, but not enough time was given between each to allow the defensive substances to be produced, or for the tissues to acquire immunity to the action of the poison. This interval varies according to the patient and to the dose given, but in general it ranges from two days for small doses up to four, five, or six days for large ones.

The second effect of tuberculin is manifested in the production of reactions, which, in their fully developed form, consist of three parts: (1) The focal reaction, manifesting itself as an inflammatory swelling around any tuberculous lesion in the body, and not simply one near the region injected. (2) The local reaction, occurring at the seat of inoculation, and exactly similar in nature to the now familiar von Pirquet's reaction. (3) The general reaction, manifesting itself as fever and the allied phenomena. With the latter we have nothing to do except to avoid it. I do not think that a severe general reaction is necessarily harmful, especially to a localized surgical lesion without secondary infection, but I think we can get equally good results in their absence. But I hold most strongly that the focal reactions are of extreme importance in the cure of tubercle by tuberculin: when violent they may, of course, be harmful, though they are not necessarily so, but when slight or moderate they are beneficial in the highest degree. When tuberculin is properly administered they should be so slight as to be unnoticeable except in the case of superficial lesions, and in particular of tuberculosis of the eye. It is for this reason I have taken such interest in the treatment of this class of case, since every effect of the remedy can be followed with precision. In such a case every dose of tuberculin, if of suitable amount, is seen to be followed in a few hours by swelling and redness of the lesion, and when this has passed off the latter is always found to have undergone improvement. To this rule I have seen no exception, and I have never yet seen a case of tuberculosis of the eye which has resisted suitable treatment with tuberculin. I should like to quote one case, an extremely severe one, recently under the care of Mr. Cargill in King's College Hospital.

The patient, a young man, aged 20, had already had one eye excised for a condition exactly similar to that from which he now suffered in the remaining eye. This showed tuberculous nodules at the sclero-corneal junction, and deposits at the back of the cornea and the angle of the anterior chamber. The iris was muddy and bound down by adhesions, and the pupil partially filled with lymph. The anterior chamber was deep, and the sclerotic injected. His vision was confined to the recognition of lights and shadows: he could not count fingers in a good light close to the eye. Treatment was commenced on October 22, 1911, with $\frac{1}{10000}$ of P.T.O., which was increased until $\frac{1}{20}$ c.c. was given on February 7, 1912. He has now gone to a convalescent home, but the treatment will be continued on his return. His condition has improved enormously, and although he is not cured

he has now a useful eye. He can read small type (Jäger 1), and his distant vision is $\frac{6}{18}$. All the nodules have disappeared, the injection of the sclerotic has gone, and the pupil is clearer. Now it was most noticeable in this patient that each injection was followed by redness and swelling of the lesions, whether there was a general reaction (which occurred two or three times) or not.

I was interested to hear Dr. Latham say that tuberculin, even in suitable doses, is often followed for a short time by an increase in the amount of sputum in cases of phthisis. I can quite corroborate this statement, and I regard the phenomenon as proof of the occurrence of a focal reaction in these patients: the sputum, which would otherwise remain in situ or come away gradually, is expelled by the swelling of the mucous membrane. In some cases there is no sputum at all except after an injection, when a single mass is expelled.

In some instances I have seen very marked improvement after a single reaction, even of some degree of violence, and though I need hardly say that I should never cause their occurrence deliberately, I have often had cause to feel glad that I have done so accidentally. But I think we can also get negative evidence of the value of local reactions from some cases in which benefit only occurs when the doses are being increased, ceasing when maximum doses, to which the patient has become accustomed, are reached. This is a case in point:—

The patient, a youth, aged 19, was admitted to King's College under Dr. StClair Thomson suffering from extensive lupoid ulceration of the nose, mouth, pharynx, and upper part of larynx. He had an ulcerated patch on each side of the nasal septum, just inside the vestibule, a similar condition on each side of the soft palate, and of the posterior wall of the pharynx on each side behind the posterior faucial pillar. This extended also to the epiglottis and the arytaenoid folds. The condition was a serious one, and was apparently spreading rapidly, but his lungs were healthy. Under these circumstances I judged it right to push tuberculin with some rapidity. I began at $\frac{1}{4000}$ of old tuberculin on April 18, 1911, and got up to 1 c.c. by June 27. During this time there were several severe general reactions, and the patient steadily improved.

He became an outpatient, and I continued with 1 c.c. each week. For more than a month mild reactions occurred after each, though not sufficient to prevent him from going on with his work, and the improvement continued. After this the patient became acclimatized, the reactions ceased, and the disease remained at a standstill, or at most

improved extremely slowly. Since September he has had injections only once a fortnight. He is now very greatly improved: the only ulcer present is a small one on the right side of the nasal septum, the left side being healthy. There is still some thickening on the posterior side of the soft palate, though none in the anterior. There is also a suspicion of the same condition in the epiglottis and right arytaenoid. I quote this case as one in which the improvement seemed to cease when the reactions did so, but I have in my own mind some doubt as to whether the lesions that are now present are actually tuberculous at all, and do not consist merely of scar tissue.

I regard the focal reaction as of so much importance that you must pardon me if I consider it in a little more detail. I do not propose to deal with the method of its production, as it is not at present fully understood, and it would lead us into some difficult problems in anaphylaxis.

First, as to the dose necessary. This varies with the degree of acquired immunity to the substance, and I believe also to the amount of antibodies in the blood. I have not been able to estimate the dose necessary to cause a reaction by employing a method of complement absorption, but from a study of my results I believe it is substantially correct to say that where the complement-absorbing power is great the early stages of the course of tuberculin may be hurried over more rapidly than when it is short, the danger of a severe reaction from small doses being much less. Apart from this we can only tell the reacting dose in a given case by trying. It may be anything from $\frac{1}{10000}$ c.c., or even less, up to 1 c.c. of old tuberculin; the latter, of course, in a patient who has been previously immunized by a course of injections.

Next, as to the relations between the local, focal, and general reactions. These vary somewhat in different patients, but as a rule the amount which will cause a local reaction round the seat of injection will also cause a focal reaction round the tuberculous lesion. Indeed, in some patients there may be a very definite though slight focal reaction where there is no appreciable effect whatever locally. I make this statement solely from my experience of eye cases, for there, as I have said before, a slight reaction is evident: when the tuberculous lesion is in a deep-seated part of the body the focal reaction, if slight, cannot be detected, and an observer studying these cases would come to a different conclusion. Even a lesion in the skin, such as lupus or a tuberculous ulcer, is not suitable for the purpose of studying these focal reactions, as a very slight and transient injection in that region is by no

means so obvious as it is in the eye. I regard the local reaction as an important clue to what is going on in the diseased area, and I aim at giving such doses at such intervals as will cause the production, after some at least of them, of a slight reaction at the area of inoculation. I give the injections in the forearm, where the effect, if any, is readily visible. Such a slight reaction as I have in my mind is unaccompanied by any noticeable general reaction or by any rise in temperature that can be detected by ordinary methods. The rule therefore is this: aim at graduating the doses so that some at least of them will cause a slight reaction only lasting from a few hours to a day, at the area of inoculation, and no rise in temperature.

I do not wish to deal at length with the way in which the focal reactions benefit the lesions in which they occur, and will content myself by saying that they cause a flushing of the tissues with fresh blood, and that they probably also stimulate the metabolism of the living cells in the neighbourhood of the tubercle bacilli, increasing their vitality and their power of resisting invaders. There is also frequently a general effect in improving the metabolism, which I believe is not a specific action. A patient should gain markedly in weight whilst undergoing a course of tuberculin, and if he does not do so the doses are probably unsuitable. This is, I believe, always the case in phthisis, but in a small uncomplicated surgical lesion which is doing well I have disregarded a moderate loss of weight without bad results.

I shall now revert briefly to the action of small doses at long intervals—such, for example, as are used by the supporters of the opsonic theory. I am far from saying that these are valueless. One case, of a large tuberculous ulcer of the arm, which I treated strictly by the opsonic method, made a great impression on me, the healing being so rapid and the resulting scar so perfect. I believe these infinitesimal amounts of tuberculin have a double action. They cause reactions, and they may also render the patient even more sensitive to the action of tuberculin than he was before. May I remind you of the extraordinarily minute amount of blood serum which may cause hypersensitiveness or anaphylaxis in a guinea-pig? According to some, as little as the one-millionth part of a cubic centimetre will alter the animal so profoundly that he may die in a few minutes after the injection of a second, larger, dose of the same serum. Exactly what is the relation between anaphylaxis and hypersensitiveness to tuberculin is as yet unknown, but there is no doubt that small amounts of the material will, under certain circumstances, render a person more

sensitive than he was before. Using these small amounts, therefore, we get one of the beneficial effects of tuberculin—the series of minimal reactions, and in this way the effect is good. But we do not get the acquired immunity both to tuberculin and to the tuberculous products formed in the body. Indeed, the patient may become hypersensitive thereto, so that the same dose of tuberculin may cause more and more marked reactions each time, and the injections, extremely small though they be, may be a source of added danger. I think it is for this reason that the opsonists have steadily lowered their doses, and we now hear of such infinitesimally small amounts as the $\frac{1}{100000}$ part of a milligramme of T.R.—and this often stale—given every fortnight.

We may avoid this hypersensitiveness by giving our doses at comparatively small intervals. Anaphylaxis takes about ten days to develop, whereas the immunizing effect is manifested in from two to five. Give a patient a dose just smaller than the reacting amount, wait for a fortnight, and repeat it; you will not infrequently find that he reacts, sometimes violently. But if you give your second injection after three or four days you will find as a rule that you can give not only the same amount but half as much again without causing a reaction. Late in the series, when the patient has attained a high degree of immunity to tuberculin, the intervals may be longer, and when you have attained 1 c.c. the intervals may be a fortnight or three weeks.

I should like to call attention to an interesting point about the reactions which may occur occasionally in persons who are partially immunized to tuberculin and who receive an injection after an unusually long interval. The reaction may occur at once, within a quarter of an hour, and may take the form of violent abdominal pain, sometimes with diarrhoea or vomiting. I believe this to be a true anaphylactic phenomenon.

Now as regards practical rules for the administration of the remedy. I think we may recognize three stages in a course of treatment:—

In the first stage we are feeling our way to the reacting dose, which, as I said before, differs greatly in different patients. We begin, therefore, with a very small amount and increase our doses as rapidly as we dare until a slight local or general reaction warns us that we are near the limit of toleration. The rapidity with which we can do this depends on the nature of the case. In lung disease we must go much more slowly than when we are dealing with localized surgical tubercle in a patient in whom the lungs are not infected, for in the latter condition a sharp reaction will do no harm, indeed, will probably be

beneficial. In long-standing cases, especially those which have come to a standstill, there is as a rule a substantial amount of immunity, and the early stage can be hurried over. In a case of phthisis I should suggest such doses of P.T.O. as $\frac{1}{100000}$, $\frac{1}{50000}$, $\frac{1}{25000}$, $\frac{1}{10000}$, and so on. In a case with a single surgical lesion of some duration I should commence with ten times this amount. As I said before, I believe that a study of complement deviation may enable us to shorten this stage somewhat, and to proceed with much more freedom. In this first stage we are preparing the way, and we should not expect much benefit from our injections.

In the second stage we aim at keeping all the time on the verge of a reaction, but without bringing about any appreciable rise of temperature. Here the increase must be very gradual, and if there is any general reaction after any dose it must be repeated until the patient is absolutely immunized to this amount before proceeding to larger. In general terms the successive amounts in a series should be somewhat in the proportion of 1, 1.5, 2, 3, 5, 7.5, and 10; thus if a patient gave a mild reaction after $\frac{1}{1000}$ c.c. I should repeat the amount until no effect was produced, and then proceed to $\frac{1.5}{1000}$, $\frac{2}{1000}$, $\frac{3}{1000}$, $\frac{5}{1000}$, $\frac{7.5}{1000}$ and $\frac{10}{1000}$, and so on, the interval after each injection being three, four, or five days. In a febrile or hypersensitive case the increase after each dose would be less, in a chronic surgical case it might be more. Each patient has to be studied separately, and no hard and fast line of treatment can be laid down.

I do not regard the method as being desirable for outpatients under the usual conditions of hospital practice, where they are only seen once a week. This is especially the case in the early stages where it is in the highest degree advisable that the temperature should be taken after each injection, and in phthisical patients, in whom an overdose may do much harm. If the earlier stages of the course can be effected in hospital and the patients got up to such doses as $\frac{1}{50}$ to $\frac{1}{10}$ c.c., the rest of the treatment may very well be done if the patient attends once a week, especially if he can be trusted to take his temperature once or twice after each injection. Even this is not always absolutely necessary, for an intelligent patient can often recognize a reaction if he has experienced one previously. But in the treatment of outpatients, however prepared, it is advisably to increase the dose very slowly.

In the third stage we aim at maintaining the high level of immunity, and here the interval between the doses may be increased. The patient is in the condition of an antitoxin horse, which will retain its immunity

for long periods if occasional doses be given. Patients in this stage, as in the throat case I have described, do not always improve, though I believe they are not likely to slip back, unless indeed from a secondary infection. I attribute this cessation of improvement to a cessation of reactions, and I think it is quite possible that it may actually be advantageous to let the patient wait for a comparatively long period between the injections, so as to let him re-attain some degree of sensitiveness. If you begin with P.T.O. or T.O.A. you may also cause these slight reactions by going on to more potent preparations such as P.T. or old tuberculin.

In conclusion, I regard tuberculin as a remedy of enormous value, but as one which is difficult to handle, so that its use should be learnt in mild cases of surgical tubercle in which no harm is likely to occur. Properly used, in most cases it gives results of the greatest value, but occasionally, like all vaccines, it proves disappointing, and one of the greatest advances we may look for in the future is the reason for its non-success and the method by which this may be avoided.

Dr. A. C. INMAN: At the Tenth International Medical Congress, on August 4, 1890, Koch made his first statement that he regarded it as a possibility to cure tuberculosis by means of active immunization. On November 13 of the same year appeared his communication on the subject under the title "Weitere Mittheilungen über ein Heilmittel gegen Tuberculose." Before applying himself to the treatment of man, Koch had carried out a series of very careful experiments on guinea-pigs. He found that he could inject subcutaneously up to 2 c.c. of undiluted old tuberculin into healthy animals without any very marked effect. When he came to consider the case in man he found this great difference: the injection of 0.25 c.c. produced the most intense reaction, whilst even a dose of 0.01 c.c. led to a mild reaction, when injected subcutaneously into a healthy adult. Man is, then, very much more sensitive to tuberculin than guinea-pigs. In the communication to which we have referred Koch definitely states: "Die wichtigste dieser Eigenschaften ist die spezifische Wirkung des Mittels auf tuberculöse Processe, welcher Art sie auch sein mögen," and nothing has since arisen to shake our faith in the specific action of tuberculin. But we have learnt one point of great practical importance—namely, that tuberculin can act on an inactive as well as an active tuberculous lesion, and that the presence in the body of an inactive latent tuberculous lesion is sufficient to determine a positive tuberculin reaction. Koch

pointed out that in non-tuberculous men, whether in good or indifferent health, no reaction, or at most a very slight one, results from the injection of 0.01 c.c. of old tuberculin. But the injection of the same dose determines, in the case of tuberculous subjects, both a well-marked general reaction and also a focal reaction. The latter is, of course, visible in surface tuberculous lesions, and can be revealed in the case of pulmonary tuberculosis by physical examination of the chest (appearance of moist sounds, &c.) and by examination of the sputum (increase or even sudden appearance of tubercle bacilli, elastic fibres, &c.). The action of the tuberculin was, according to Koch, to kill not the tubercle bacilli, but tuberculous tissue; and further, it had no effect on dead tuberculous tissue—caseous masses, necrotic bone, &c.—nor on the tissue killed by its own action. Continuing his experiments, Koch found that active immunization with old tuberculin had no effect on the tubercle bacilli themselves; he was dealing with a “tuberculin immunity” and not with an immunity against the bacteria. With a view to remedying this defect he experimented further, and his next preparation was an alkaline extract of tubercle bacilli (T.A.) which he had to discard because the body was unable to absorb more than a certain mass of dead tubercle bacilli at any one spot, resulting in abscess formation at the site of injection. By finely powdering the bacilli and then centrifugalizing, he obtained his next important preparation, Tuberculin T.R. (*Tuberkelbacillenrückstand*), which he found possessed undoubted immunizing properties, and, what is very important indeed, these were independent of reactions, although sufficiently large doses could, in the tuberculous subject, lead to reactions.

This was a most important advance; here was an actively immunizing agent which proved effective by stimulating the production of immune substances without necessarily producing febrile, local, or focal reactions. Now the former preparations, old tuberculin, T.A. and T.O., depended for their curative effect on the production of such reactions, whilst in the case of tuberculin T.R. all reactions should, and in most cases can, be avoided until the patient is immune against very large doses, and also, as Koch was able to affirm, against the tubercle bacilli themselves. Further, Koch was able to show, and this has been fully substantiated since, that a man immunized against tuberculin T.R., even though all reactions have been excluded during the course of injections, does not react any longer to large doses of old tuberculin. It remains to be added that Koch's last preparation, wherein he embodies the whole properties of the dead tubercle bacillus as an actively immunizing agent

was a simple suspension of comminuted tubercle bacilli in physiological salt solution (Tuberculin-Bacillen Emulsion); in other words, what we have become accustomed to speak of, since the epoch-making teachings of Wright, as a vaccine or antigen. It will be granted by all who have worked on the experimental side of the question that it is not a perfect antigen, inasmuch as it has been found impossible by its means to immunize animals against a later infection by living bacteria. Before turning to what I believe to be the true explanation of the results obtained by tuberculin treatment, I would follow out the line of thought which Koch followed in his researches. I am convinced, from reading Koch's papers, that he fully recognized the importance of, and longed for a guide to, the individual treatment of the patient, for such a guide as has been granted to us by the genius of Wassermann in the case of syphilis. Witness the joy with which Koch welcomed the discovery of the serum-agglutination phenomenon as a possible means of measuring the immunizing response of the individual. Henceforth he hoped that the way would be made clear, making it possible to treat each case individually, to watch the effect of each injection, and to obtain evidence of successful immunization. These same thoughts stimulated Wright to all those works which have raised him to the front rank of medical scientists, and have led to the introduction of active immunization as a therapeutic agent in the treatment of most bacterial infections. How fully Koch realized the significance of the immunizing response on the part of the healthy tissues is evident from the support he gave to a paper read by Götsch in 1901. The latter was advocating the careful treatment of pulmonary tuberculosis by tuberculin with avoidance of all reactions, general or local, and Koch, at the end of the paper, stated that: "I can, from my own experience, agree that it is necessary to avoid all more marked reactions."

Let us recall that, in the memorable days of 1891, Koch himself noted that, in the case of lupus, tuberculosis of glands, bones, and joints, the injections of old tuberculin led to rapid healing in slight cases and slowly increasing amelioration in bad cases, whilst he definitely stated that, in contrast with these cases, patients with advanced pulmonary tuberculosis are much more susceptible to tuberculin than those with "surgical" tuberculous infections. Has not the later work, made possible for us by the researches of Wright, given us an explanation, of far-reaching importance, as to the difference between such localized tuberculous infections and the graver, truly generalized tuberculous infections exemplified by advancing tuberculosis of the lungs?

In the first instance Wright, and subsequently Bulloch, examined cases of localized bacterial infections, their series comprising, as far as tuberculosis is concerned, chiefly cases of so-called "surgical" tuberculosis. The net result of these experiments was to establish the fact that in the majority of such cases the opsonic index was constantly below the normal, as is clearly shown in the following table:—

Disease	Number of cases	Opsonic index (average)
Lupus or skin tuberculosis	150	0.75
Lupus ...	3	0.65
Tuberculous abscess	3	0.53
Healthy adults {	66	0.95
{	20	1.01

(Wright and Bulloch.)

Later it was established that this low index could be raised not only by the inoculation of appropriate doses of tuberculin, but that a transient rise of the index could be obtained by sufficiently disturbing the focus of infection by means of massage, Bier's hyperæmia, Finsen light, &c. When cases of acute tuberculosis—acute miliary, tuberculous meningitis, &c.—came to be studied, it was found that instead of a constantly low index being the rule, very high indices might be found, and what is very important, the readings of the opsonic indices varied considerably from day to day, or even from hour to hour. These tests have now been applied to a large number of cases of pulmonary tuberculosis, and we find that tuberculosis of the lungs may be localized or generalized. An examination of 250 consecutive cases of doubtful pulmonary tuberculosis gave indices varying outside the normal limits in 159 cases: 97 started low, and of these 56 rose as the result of exercise and 41 remained low after exercise; 62 started high, and of these 54 fell after exercise and 8 remained high after exercise; whereas in the cases which started low 42 per cent. were uninfluenced by the exercise, only 12.9 per cent. of those starting high remained high after exercise, whilst 87 per cent. fell after exercise.

I have already suggested that low indices remaining low or rising after exercise should be considered evidence of active localized tuberculosis when taken in conjunction with clinical signs and symptoms suggesting pulmonary tuberculosis, and that under similar circumstances high indices should be taken as evidence of an active tuberculous lesion which has more ready access to the lymph- and blood-stream. When we come to investigate the manifestly active and advancing cases of pulmonary tuberculosis we find continually varying indices—daily

or even hourly variations, just as we have daily or even hourly variations in the temperature chart. Such lesions then have ready access to the lymph- and blood-streams, and a continual war is being waged between the tubercle bacilli and their products on the one hand and the defensive forces of the blood and tissues on the other. Let us now consider the effect of injecting tuberculin into patients falling under these various groups. Let us imagine in the first place that a dose of old tuberculin is injected, sufficiently large to cause the focal reaction referred to above—hyperæmia, swelling, necrosis of the living tuberculous tissue—in the case of a small localized focus in the lung; localized, but, it must be admitted, so potentially dangerous. It can be readily imagined that such a focal reaction taking place, the dose of tubercle bacilli or their products entering the system is not more than the defensive forces of the body can cope with. After a temporary period of intoxication the body reacts and gains the upper hand, and this process may conceivably be repeated until nothing is left of the tuberculous tissue, its place being taken by a fibrous tissue scar, which remains to mark the site of the victory of the body over the bacilli. Nature is in the habit of thus dealing with bacteria, when she, unaided, gains the upper hand of a bacterial invasion.

In our hypothetical case Nature has been helped by means of specific stimulation to react and thus to resist an invasion she was unable to overcome by herself. Proceeding a step further, we can conceive that in the event of the lesion being in more ready communication with the lymph- and blood-stream, more potent for evil by reason of size or content of virulent bacilli, the inoculation of a similar dose of tuberculin may cause an outpouring of bacteria or their products in such a dose or doses that the body is unable to react sufficiently quickly or effectively so as to secure immunity. A repetition of the dose can only make matters worse, and I believe that this is the most reasonable explanation of the failures, nay, even disasters, formerly met with in the course of tuberculin injections. This being so it follows that the proper selection of cases and the correct dose for each individual case is of paramount importance.

Koch urged the profession to adopt all measures at their command to make the earliest possible diagnosis of the disease. It is regrettable that even to-day the examination of the sputum for the presence of tubercle bacilli is too often neglected until it is too late. The sputum should be examined carefully as a routine procedure in all cases of cough accompanied by expectoration. At the same time it must be

fully recognized that before the stage of ulceration of a tuberculous lesion of the lung the focus of disease has been actively progressing for some time. Our efforts for some years past have been directed to finding some means of diagnosing closed tuberculosis of the lung in its earliest stages. Koch suggested that the hypersusceptibility to injections of old tuberculin of tuberculous subjects offered a means of the precocious diagnosis of the disease. Much time and work has been devoted to this question since then, and we are, I think, now in a position to state that whereas the tuberculin reaction is truly specific in character it cannot discriminate *per se* between an active and a latent inactive tuberculous lesion.

Extended researches on the tuberculin reaction as occurring at the various periods of life in human beings show that in a large percentage of cases the adult human being cannot be considered as an animal free from all tuberculous infection. Between the years 1830 and 1900 a number of post-mortem statistics as to the frequency of tuberculous infection in man were published, notably those of Bollinger and Müller, Simmonds, Schwer and Boltz, Kossel, Küss, Schlenker and Hutinel, most of which showed a marked degree of conformity. During the first months of life the percentage of tuberculous cases was about 1, at the end of the first year it had risen to 12, and by the fourth year to about 40. These observations culminated in the classical statistics of Naegeli in 1900, which have stood the test of time to the present day. Naegeli systematically examined 500 consecutive cadavers of all ages for the presence of tuberculous lesions. It is interesting to note that as he became more adept during the course of the investigation he was able to find evidence of tuberculosis more frequently. Thus whereas his total percentage of positive results in the case of adults is 93, during the last 300 post mortems the percentage of tuberculous lesions was 98, which probably represents the correct figure for the hospital classes.

			Number of post mortems	Free from tuberculosis	Tuber- culous	Per- centage	Fatal tubercu- losis	Per- centage	Non-fatal tuberculosis	Per- centage
Subjects	under	18	88	73	15	17	11	73.3	4	26.7
Adults	420	29	391	93	110	28	281	72

After Et. Burnet's "La Tuberculose de l'enfant à l'adulte," *Bull. de l'Inst. Pasteur*, 1911, ix.

From the above table, summarizing the results obtained by Naegeli, we see that under the age of 18 years tuberculosis is relatively uncommon and is fatal in 73·3 per cent. of cases, whilst in the adult tuberculosis is common, but largely latent and non-fatal.

The study of the tuberculin test enables us now to investigate the child and adult during life, and a number of figures are available. Von Pirquet, with the technique devised by him—the cutaneous tuberculin test—was the first to publish a series of valuable figures on the subject. He submitted 693 clinically non-tuberculous children to the cutaneous test, with the following percentage of positive results:—

During 1st year...	3 per cent. reacted positively.
.. 2nd	2 ..
.. 3rd and 4th years	13 ..
.. 5th and 6th	17 ..
.. 7th to 10th	35 ..
.. 11th to 14th	55 ..

The following table, drawn up by Et. Burnet, gives a comparison between results of post-mortem examinations and the tuberculin tests:—

	POST-MORTEM (GIRON)		TUBERCULIN TESTS			
	Fatal and non-fatal tuberculosis	Minimal number of non-fatal tuberculous cases	Cutaneous test, 25 per cent. tuberculin, von Pirquet	Modified tuberculin test, Ganghofner	Stich reaction alone Hamburger	Stich reaction and subcutaneous test Monti
2nd year ...	40	17	2	12	9	9
3rd and 4th years	60	30	13	27	23	27
5th and 6th ..	56	34	17	47	36	51
7th to 10th ..	63	35	35	57	47	71
11th to 14th ..	70	53	55	70	51	94

It is interesting to note that Comby inoculated large doses of tuberculin into clinically healthy infants without reaction. To summarize the results, children, not born of mothers in an advanced stage of tuberculosis, come into the world in most cases free from tuberculous infection. As each year advances a progressive number becomes infected, until at the age of puberty a total of one-half is reached. By the time he is adult practically every individual is the bearer of a

tuberculous lesion. It is important to bear these facts in mind when considering any results of the injection of tuberculin into the human body.

We have heard from Dr. d'Este Emery that, employing the method of complement fixation, he finds in the serum of the majority of adults the presence of specific antibodies to the tubercle bacillus, but not to other pathogenic micro-organisms. The researches of Franz are very important in this connexion. This observer took 400 apparently healthy soldiers of a Bosnian regiment in 1901 and gave them all injections of Koch's old tuberculin, with a maximum dose of 0.003 c.c.; 61 per cent. of these men gave a positive reaction. Next year (1902) 100 of these soldiers were again inoculated, with the result that all those who had reacted the previous year reacted again, and in addition fourteen others, making 76 per cent. altogether. Three hundred and twenty-three men were inoculated for the first time in 1902, and 68 per cent. reacted positively. This regiment is recruited from a district in which tuberculosis is rife, so Franz inoculated in a similar way a number of men in a Hungarian regiment which is recruited from a district poor in tuberculous cases, yet 38 per cent. gave a positive reaction. The same author followed out the subsequent history of the men inoculated and publishes the following interesting statistics:—

Regiment	Date of inoculation	Number of men inoculated	Reaction	During the three years' service were discharged through death, ill-health, or excessive leave due to—		
				Tuberculosis	Suspected tuberculosis	Other diseases
Bosnian Infantry Regiment No. 1	1901	400	(+ 245 (61 per cent.) - 155 (39 " ")	17 (8 deaths) 5 (4 " ")	22 25	10 7 (1)
Ditto	1902	323	(+ 222 (68.8 " ") - 101 (31.4 " ")	13 (6 " ") 4	28 (1) 13	7 (2) 5
Infantry Regiment No. 60	1902	279	(+ 108 (38.7 " ") - 171 (61.3 " ")	4 3 (2 " ")	4 5	8 12
Total	...	1,002	(+ 575 - 427	34 (14 deaths) 12 (6 " ")	54 (1) 43	25 (2) 24 (1)

I would also draw your attention to the very interesting observations of Metchnikoff, Burnet and Tarassévitch, which appeared in the *Annals of the Pasteur Institute* of November, 1911.¹ In this research the authors took advantage of the fact that tuberculosis is very

¹ *Annales de l'Institut Pasteur*, 1911, xxv, pp. 785-804.

rare among the Kalmouks, who inhabit a certain area of the Russian steppes, excepting at the periphery of this area, where the tribe is in contact with the Russians and the tuberculosis incidence among the Kalmouks and the Russians is practically identical. The Kalmouks who live on the steppes, mostly in the open air, have practically no

	Number of cases	Positive	Negative
C.P.T. No physical signs ...	71	45	26
Physical signs, but no T.B. in sputum ...	54	44	10
Physical signs, with T.B. in sputum ...	15	13	2
No physical signs, with T.B. in sputum ...	1	1	—
Fibrosis of lung ...	13	11	2
No evidence of tuberculosis ...	24	—	24
Acute tuberculosis ...	2	2	—
Tuberculous adenitis ...	7	6	1
Pneumonia (unresolved) ...	2	2	—
Bronchitis ...	15	—	15
Bronchitis and asthma ...	5	1	4
Bronchiectasis (? tuberculosis) ...	6	2	4
Pleurisy... ...	5	3	2
Pleurisy (old) ...	3	—	3
Pleurisy with effusion ...	11	10	1
Empyema (old) ...	1	—	1
Mitral regurgitation and stenosis ...	6	—	6
Aortic aneurysm and C.P.T. ...	1	1	—
Malignant endocarditis ...	1	—	1
Mediastinal neoplasm ...	1	—	1
Lymphadenoma ...	2	1	1
Addison's disease... ...	1	—	1
Exophthalmic goitre, with physical signs of quiescent tubercle ...	1	1	—
Dyspepsia ...	1	—	1
Gastric ulcer ...	1	—	1
	250	143	107

	Number of cases	Positive	Negative
Clinically tuberculous disease ...	56	48 (85.71 per cent.)	8 (14.28 per cent.)
Doubtfully tuberculous disease ...	134	91 (67.91 ")	43 (32.08 ")
Clinically non-tuber- culous disease ...	60	4 (6.66 ")	56 (93.33 ")

natural resistance to tuberculosis, and it is noticeable that those of them who come into towns, and thus into contact with phthisical individuals, rapidly succumb to the disease. Tested with the cutaneous tuberculin method of von Pirquet, only one-half of the young Kalmouks entered as first-year students at Astrakhan gave a positive reaction, while the senior students who had been in residence for more than one year gave a positive reaction in nearly every case. The mortality from tuberculosis among the Kalmouks who went to Astrakhan to study used

to be appalling, but as tuberculosis spread amongst them they have gradually become more resistant. In fact, we have a repetition of the conditions in Europe as affecting infants who have not yet acquired immunity or resistance to tuberculosis, and adults, most of whom are infected with tuberculosis but show a considerable degree of acquired immunity against the tubercle bacillus.

Extended observations have led me to the conviction that the tuberculo-opsonic index test, conscientiously carried out and intelligently applied, offers us a satisfactory method of diagnosis of active tuberculous disease in the early stages. All methods of diagnosis, and this is by no means confined to tests carried out in the laboratory, are liable to error, but I am convinced that, when properly carried out, the tuberculo-opsonic index can give us valuable and timely information. The foregoing table, dealing with 250 cases, is taken from the Medical Report of the Brompton Hospital for 1910.

This method has been considered in more detail in a lecture on the Specific Diagnosis of Pulmonary Tuberculosis which appeared in the *Lancet* of December 17, 1910.

THE SELECTION OF CASES FOR TUBERCULIN TREATMENT.

In 1908 I suggested that Turban's classification of pulmonary tuberculosis was not satisfactory from the point of view of selection of cases for treatment, inasmuch as it dealt rather with the stage of the disease as revealed by physical examination of the chest than with reference to temperature or to specific serum reactions, which are the most important guides to the degree of activity of the disease. The following classification was suggested for the purpose:—

Class I: *Resting febrile*. Cases with fever at rest in bed.

Class II: *Ambulant febrile; resting afebrile*. Usually a transition stage between Classes I and III.

Class III: *Ambulant afebrile*. Cases without fever in spite of exercise or work.

In tabular form this classification may be shown thus:—

	Clinical		Pathological
Class I.	Resting febrile,	...	Excessive auto-inoculations occurring spontaneously
Class II.	Ambulant febrile, resting afebrile	...	Excessive auto-inoculations inducible by exercise
Class III.	Ambulant afebrile	...	Appropriate auto-inoculations inducible by exercise

We will take Class III first, inasmuch as it is at once the simplest from the point of view of analysis and comprises the majority of the cases which are suited to specific treatment. Ambulant afebrile, cases without fever, in spite of exercise or work; this naturally includes a wide range of cases, from those which are only able to indulge in very moderate walking exercise without determining febrile reactions to those which are able to do work, even of a strenuous manual nature, without any rise of temperature above the normal. The treatment of such cases by carefully graduated labour has been successfully accomplished by Paterson at the Brompton Hospital Sanatorium, and a series of examinations of the tuberculo-opsonic indices of patients undergoing the treatment showed that the need for the most careful graduation of the labour, both in point of sufficiency and limitation, depended on the fact that the movements induced auto-inoculations of tubercle bacilli or their products. For a detailed account of this most interesting adjunct to the sanatorium treatment of afebrile ambulant patients, which confirms and amplifies the teachings of Brehmer and Walther, I commend to your notice Dr. Paterson's book on "Auto-inoculation in Pulmonary Tuberculosis."

The tuberculosis of the lung in these cases of Class III may be "open" or "closed," and the extent of the lesion as revealed by physical examination of the chest may be limited to a portion of one lobe, or may involve three or four lobes.

What is the best treatment for cases of this class? The possibilities are (a) to subject them, under skilled medical supervision, to a course of carefully graduated labour as advocated by Paterson at Frimley; (b) to treat them as outpatients with drugs and preparations destined to alleviate symptoms and support the strength of the body; (c) to treat them as outpatients with tuberculin, with the object of eradicating their disease by a process of active immunization against the specific cause; (d) by a combination of sanatorium and tuberculin treatment. Now for the comparison between any forms of treatment certain data are required, and these are unfortunately not always forthcoming, however much they are to be desired. In the present instance, the data are incomplete, but such as they are, they are not devoid of interest. At present the only data of results obtained by the Frimley method are to be culled from Paterson's book, "Auto-inoculation in Pulmonary Tuberculosis," Appendix IV.

PATIENTS TREATED DURING 1908.

Classification on leaving	Total in each class	At work, February, 1911	Not at work	Unreported, February, 1911	Dead
Arrest ...	137	97	6	27	7
Arrest + T.B. ...	60	33	7	6	14
Improved ...	24	12	3	2	7
I.S.Q. or worse ...	19	4	3	9	3
Died (0·8 per cent.) ...	2	—	—	—	—
Total ...	242	146	19	44	31
Percentages ...	—	60·3	7·9	18·1	12·8

As far as I know, there are no trustworthy figures to show the lasting results of hospital treatment. The treatment with tuberculin in the outpatient department has recently been strongly recommended by Camac Wilkinson. An analysis of the records of 246 cases treated between 1902 and 1906 and reported as well in 1908 reads as follows:—

Turban	Number of cases	Number of cases having temperature above normal before treatment	Tubercle bacilli present
Stage 1 ...	115	18	5
" 2 ...	74	31	41
" 2-3 ...	40	17	37
" 3 ...	17	10	14
Total ...	246	76 (30·8 per cent.)	97 (39·4 per cent.)

Date of treatment	Percentage well in 1908			
	Stage 1	Stage 2	Stage 2-3	Stage 3
1902 ...	100	50	50	50
1903 ...	100	100	66	0
1904 ...	100	100	100	" All marvellously well "
1905 ...	100	100	100	45
1906 ...	100	90	50	30 improved

These cases were treated with large doses of tuberculin and the majority were subsequently tested with maximum doses of old tuberculin. They must, of course, be regarded as specially selected cases, and even then I do not know of any similar figures in the literature dealing with the treatment of pulmonary tuberculosis. The lack of a sufficient number of control cases makes it impossible to draw any definite conclusions as to the value of the method advocated.

The combination of tuberculin with sanatorium treatment seems to have advantages, as is shown from the figures recently published by Loewenstein. The satisfactory feature of these figures is that they deal with the percentage of loss of tubercle bacilli at the end of treatment. Loewenstein computes that in the case of patients undergoing the usual

hygienic-dietetic treatment of the German sanatoria, not more than 20 per cent. lose their tubercle bacilli from the sputum at the end of the treatment. His cases numbered 682, all of them with tubercle bacilli present in the sputum. They were all treated with tuberculin until they had attained immunity to 10 mg. of old tuberculin or 0.01 mg. tuberculin B.E. At the end of treatment only those cases are counted as having lost their tubercle bacilli in which the sputum was examined four times (antiformin) and after an injection of tuberculin, with a negative result.

SIX HUNDRED AND EIGHTY-TWO CASES WITH TUBERCLE BACILLI PRESENT.

Treated with	Number of cases	Lost tubercle bacilli
Old tuberculin ...	409	237 = 57.94 per cent.
New tuberculin ...	204	86 = 42.15 "
Old and new tuberculin ...	69	38 = 55.07 "
Total ...	682	361 = 52.93 "

He draws attention to the fact that the last group consisted almost without exception of grave cases of the second and third stages.

Bandelier's figures, which appeared in 1910, dealing with 202 cases of open tuberculosis of the lungs treated with tuberculin, gave 63 per cent. loss of tubercle bacilli. In the published records dealing with 1,000 cases treated with tuberculin, 56 per cent. lost their tubercle bacilli.

Again, when we consider lasting results we find the balance in favour of tuberculin. Szaboky's figures are interesting in that he compares cases treated (*a*) in a sanatorium, (*b*) in a general hospital in Budapest, (*c*) with tuberculin with open air.

He was following Spengler's method of treatment with *Perlsucht* and Human Old Tuberculin.

Stage	SANATORIUM			HOSPITAL			COMBINED TREATMENT		
	Improved	I.S.Q.	Worse	Improved	I.S.Q.	Worse	Improved	I.S.Q.	Worse
I	62.5	35.5	2.0	50	50	—	75	25	—
II	21.6	59.5	18.9	25	25	50	33.3	16.6	50.1
III	11.6	38.7	50.0	7.7	30.8	61.5	28.5	35.7	35.7

These figures will suffice to show that those who have had considerable experience with tuberculin consider that it offers advantages over the

hygienic-dietetic treatment; in fact, after perusing the literature on the subject one is left impressed with the unanimity of this opinion. At all events it would hardly be denied that the time has now come when it is desirable to test a large number of cases in such a way as to leave no doubt as to the indisputable superiority of the method. The only difficulty is to decide on the best method of administering tuberculin. There may be said to be three methods which have each their advocates: (a) The method of rapid tuberculin immunization with old tuberculin; for this to be efficacious reactions must be produced and the patient must be treated until he fails to react to large doses (1 c.c. old tuberculin). (b) The method of gradually increasing doses of tuberculin T.R. or B.E., avoiding, as far as possible, all febrile reactions until the patient can tolerate large doses (5 to 10 mg. B.E.), and fails to react to large doses of old tuberculin. (c) The method of initial minimal doses, with the rigid avoidance, as far as possible, of febrile reactions, the dose being regulated with reference to the temperature chart, a low, "flat" temperature being regarded as evidence of a satisfactory response on the part of the body. No dose is increased so long as it has still an effect on the temperature; when this is no longer the case an increase is made to the next dose which has the desired effect. In this way the increase of the dose is in many cases very slow, but all the time the patient is kept under the influence of tuberculin. It is important, both on theoretical grounds and by analogy with our experience in cases of tuberculous glands of the neck, &c., to continue the treatment for a long time, eighteen months to two years, and for some time after all symptoms have disappeared. At the end of the course the patient should be able to tolerate full doses without reaction.

Now as to the relative merits of these three methods. In strictly localized, especially closed, cases I can see no theoretical or practical objection to the treatment by focal reactions induced by injections of old tuberculin any more than I can to the treatment of superficial tuberculous lesions by means of the Finsen light, &c., nor to the treatment of other localized tuberculous lesions by means of Bier's passive intermittent hyperæmia.

The rapid immunization with tuberculin T.R. or B.E. until large doses are tolerated without a single reaction having occurred during the course—and this is comparatively easily achieved in ambulant afebrile cases presenting the physical signs of Turban's stage II and III—leads often to distinct rapid amelioration of the general conditions. But I have not seen a single case in which the method can be said to have

led to arrest; indeed, it is difficult to see how any extensive area of disease can become healed in so short a time—three to four months. For this reason, and seeing that the treatment is individual and that each dose is allowed to have its effect, I prefer the method of a long course of new tuberculin, the doses being regulated with reference to the temperature chart and general condition of the patient. Reference to the tuberculo-opsonic index intelligently applied can, during such a course, from time to time give valuable information, when considering the advisability of increasing the dose.

Class II: Ambulant Febrile, Resting Afebrile.—The valuable lesson learnt from a study of the blood in relation to the effect of exercise on the tuberculo-opsonic index gives the key to the appropriate immediate treatment of cases of this class. All movements, active or passive, which may cause an auto-inoculation must, as far as possible, be abolished. Paterson has shown in a striking way the value of absolute rest in reducing fever due to excessive auto-inoculations. In some cases attention to rest is all that is required to convert a case of Class II into one of Class III (ambulant and afebrile), but this is unfortunately not always so. Small doses of tuberculin T.R. or B.E. may in these cases give satisfactory results.

Class I: Resting Febrile.—This class includes a wide range of cases, from those with extensive advanced disease to those with active commencing tuberculosis. It is hardly conceivable that the former can ever be benefited by tuberculin; the tissues generally are abnormal and the lungs not infrequently a series of abscess cavities. It has been my good fortune to see a few cases of acute tuberculosis apparently benefit to a remarkable degree from the use of small doses of tuberculin.

The fever associated with this last class naturally suggests the question of secondary bacterial infections in pulmonary tuberculosis, a question of vital importance in connexion with the specific treatment of the disease. Actually in 1890, Koch drew attention to the fact that tuberculin was powerless to act against bacteria other than the tubercle bacillus. It must always be borne in mind that in every case of open tuberculosis of the lung the possibility, nay the likelihood, of a secondary infection exists. It was commonly believed that fever indicated the presence of a secondary infection, but this has been proved inaccurate. In some cases the fever is doubtless due to the tubercle bacillus itself, whilst in other cases with a normal temperature there may be a secondary infection. We are all familiar with the fever which occurs during the active period of a pure

tuberculous pleurisy, as also are we with the afebrile course of many infections due to the pneumococcus, the staphylococcus, &c., even in diseases of the respiratory tract—chronic bronchitis for instance. In a series of examinations of patients suffering from various stages of open pulmonary tuberculosis we found evidence of secondary infections in 87·5 per cent. of febrile cases, and in 54·1 per cent. of afebrile cases. The figures were as follows:—

Subdivisions	Febrile		Afebrile	
A. Infection by T.B. and secondary organisms	...	28 (87·5 per cent.)	...	13 (54·1 per cent.)
B. Infection by T.B. alone	...	4 (12·5 ..)	...	10 (41·6 ..)
C. Infection by secondary organisms alone	...	—	...	1 (4·1 ..)
Total	...	32	...	24

It behoves us, then, before embarking on tuberculin treatment, to examine for the presence of a secondary infection. In advanced cases, even were it possible to treat the tuberculous infections specifically, the presence of secondary infections almost precludes the hope of any amelioration from specific treatment. But in earlier cases it may prove to be possible to support the tuberculin treatment by specific treatment directed against the other bacteria.

In conclusion, I would urge that we now have certain data and facts to work on, and that the time is ripe when a combined action in our larger hospitals for consumption and our sanatoria should be set in motion with a view to settling the value of the much debated tuberculin treatment of pulmonary tuberculosis. Koch recommended those who would embark on tuberculin therapy to confine themselves in the first instance to the simpler forms of localized tuberculosis. Similarly, Wright, in his "Studies on Immunization," says: "Setting our hearts upon the immediate discovery of a, shall I say, cure for . . . advanced consumption . . . we fail to reflect that . . . in this (case) we have probably a multiform mixed infection complicated with what are in effect voluminous open abscesses . . . and aspiring after a remedy . . . we have neglected to work at the comparatively simple and soluble problems of localized diseases."

I suggest that it would be profitable from a point of view of settling the point at issue to experiment in some such way as the following:—

(1) Ambulant afebrile cases: (i) open tuberculosis, (ii) closed tuberculosis.

The following tests should be performed after the patient has been under observation for at least a week :—

(a) Opsonic index test before and after approximate exercise. The results to be classed under headings :—

- (A) Index low before, but rising after exercise.
- (B) Index low before and after exercise.
- (C) Index high before and rising after exercise.
- (D) Index high before and after exercise.

(b) Tuberculin subcutaneous test.

It must be carefully noticed whether in the event of a positive reaction there is (i) febrile reaction, (ii) local reaction, (iii) focal reaction, and at what dose of tuberculin the reaction occurs.

(c) The extent of disease as revealed by a (i) physical examination and (ii) X-ray examination of the chest.

This should be done on every ambulant afebrile case admitted over a certain period, and alternate cases only treated with tuberculin.

(2) In view of the published reports of Loewenstein, Bandelier, &c., quoted above, it would be desirable to treat all cases of tuberculosis of the lung having still tubercle bacilli in the sputum after having undergone sanatorium treatment with tuberculin, to test whether such a procedure would not diminish that lamentably large class of results classified as "arrest with persistence of tubercle bacilli."

A certain amount of discussion has recently arisen in the medical press as to the advisability of carrying out the tuberculin treatment of pulmonary tuberculosis under strict medical supervision, such as is only obtainable in institutions in the case of the poor, or at considerable expense in the homes of the wealthy, or at tuberculin dispensaries. In this connexion I cannot refrain from quoting Koch's own words, as they express so well the rational point of view: "Ueberhaupt möchte ich dringend davon abrathen, das Mittel (Tuberculin) etwa in schematischer Weise und ohne Unterschied bei allen Tuberkulösen anzuwenden. Am einfachsten wird sich voraussichtlich die Behandlung bei beginnender Phthise und bei einfachen chirurgischen Affectionen gestalten, aber bei allen anderen Formen der Tuberculose sollte man die ärztliche Kunst in ihre vollen Rechte treten lassen, indem sorgfältig individualisiert wird und alle anderen Hilfsmittel herangezogen werden, um die Wirkung des Mittels zu unterstützen. In vielen Fällen habe ich den entschiedenen Eindruck gehabt, als ob die Pflege, welche den Kranken zu Theil wurde, auf die Heilwirkung von nicht unerheblichem Einfluss war, und ich möchte deswegen der Anwendung des Mittels in geeigneten

Anstalten, in welchen eine sorgfältige Beobachtung der Kranken und die erforderliche Pflege derselben am besten durchzuführen ist, vor der ambulanten oder Hausbehandlung den Vorzug geben. In wie weit die bisher als nützlich erkannten Behandlungsmethoden, die Anwendung des Gebirgsklimas, die Freiluftbehandlung, spezifische Ernährung, u.s.w., mit dem neuen Verfahren vortheilhaft combinirt werden können, lässt sich augenblicklich noch nicht absehen; aber ich glaube, dass auch diese Heilfactoren in sehr vielen Fällen, namentlich in den vernachlässigten und schweren Fällen, ferner im Reconvalescenzstadium im Verein mit dem neuen Verfahren von bedeutendem Nutzen sein werden."

In conclusion, let me urge upon those who would embark upon the tuberculin treatment of pulmonary tuberculosis to make themselves acquainted with the original papers of Koch, to study carefully the progress which has been made since 1890 in the study of immunity, and to take the advice of the introducer of the principles of active immunization into practical medicine, and study cases of localized tuberculosis first before proceeding to the treatment of that complex disease, pulmonary consumption.

Dr. S. VERE PEARSON: I shall leave the details of exactly how and when to use the tuberculins to others with a larger experience of their use. I shall confine my remarks to the expression of a few opinions of a general character—opinions to which the experience I have had has led me. My experience is almost entirely confined to the use of Koch's human tuberculins, T.R. and B.E., and chiefly to the former. I have given these both by mouth and by hypodermic injection, perhaps rather more frequently by the former method than by the latter. Tuberculin is a remedy of undoubted value for pulmonary tuberculosis; it is a remedy which may do good, but can do harm, therefore it is essential that it should be given cautiously. I have occasionally tried the remedy cautiously in cases having a thoroughly bad outlook. I have not yet seen any remarkably good results from its use under such circumstances; in fact, so far as my experience has gone in this respect I have found the remedy disappointing. At the present moment I do not feel competent to lay down full and precise rules on the choice of patient and all that is involved under that head. But this I will say, it is not necessary to give tuberculin, or any other remedy, to people with perfectly healed lesions. This seems almost too obvious to need statement; yet I think it is worth stating at the present moment, because there seems to be a tendency in some quarters to

consider it expedient to treat those diagnosed as having tuberculosis almost solely from the fact that they give a positive reaction to the subcutaneous injection of old tuberculin.

The next point upon which I wish to insist is, that when one of the tuberculins is being administered, or for that matter any other remedy, it is advisable to take rectal rest temperatures at least twice daily in the case of all patients who have active disease, or whose disease has recently shown even a tendency to activity. In fact this is, in my opinion, almost essential. Such readings are certainly advisable. But there is another kind of observation; I refer to readings of the opsonic index, which is impracticable: not only so, but I consider these readings are not a necessary aid to the administration of tuberculin.

I desire this afternoon to dilate especially upon what I fear may be a danger of the present state of affairs in respect to the use of tuberculin, in the treatment of pulmonary tuberculosis. When tuberculin is being administered it is particularly important that attention be directed to the methods of living, especially as to fresh air and food, and as to the mode and extent of spending exertion. It is especially important to emphasize attention to such matters, otherwise both physician and patient may defeat the aims and ends of medicine by undue dependence upon the specific remedy to the, at least, partial neglect of other more important measures. This side of the subject has a bearing not only upon the cure of the particular member of the community under the care of the physician, but also upon the wider medical sphere of preventing and eradicating the disease, and I feel that there is some danger to be avoided at this present juncture lest undue attention to the use of a remedy of proved efficacy against tuberculosis may actually become a stumbling block in the path of eradicating the disease.

Clinical physicians are apt to think sometimes too exclusively of the individual patient to be cured. Attention must not be unduly distracted from the detection, exposure and elimination of the bad hygienic circumstances causing the malady. Undue concentration upon any form of treatment which is applied while the patients continue to live under ordinary home conditions, fails to help forward many other hygienic, moral and social blessings, beside the blessing of eradicating tuberculosis, and its ultimate eradication becomes less certain. It is necessary, therefore, to beware of anyone who under present circumstances advocates any such line of attack while belittling more far-reaching methods.

Again, therapeutists are apt to think too exclusively of the medicine or vaccine prescribed. I do not advocate withholding any such remedy of proved efficacy for the sake of emphasizing the advice I give, unless I am quite convinced that thereby the patient gains. Undoubtedly he does so gain, not infrequently, and this should be fully realized by all therapeutists who use the tuberculins. I maintain that in the case of some patients, the chances of making a good and permanent cure are bettered by abstaining from giving tuberculin. Suppose, for example, the patient to be a young man, who is of a lively disposition, and without severe symptoms or appreciable feelings of ill-health, and that he stays only two or three months in a sanatorium, or under close medical supervision elsewhere, he will learn more quickly and thoroughly how to get, and keep, well if he is soon and thoroughly taught what precautions he must take; and this is more easily accomplished if tuberculin is not given, at all events for some time. He is much too apt, if given tuberculin from the start, to ascribe all improvement to that remedy, and to realize insufficiently the amount of care of himself he must necessarily take.

I have come to recognize that so far as gaining "kudos" and making money is concerned, both amongst rich and poor, it often pays better to be administering some remedy, especially such an one as a vaccine, the hypodermic injection of which carries a certain amount of mystery and romance, and a slightly complicated technique with it, than to be giving sound advice on the method of living. A patient is more impressed by the hypodermic injection of vaccine than by an instruction to walk a certain distance, even though the latter, given as a therapeutic measure in the all important regulation of rest and exercise, may be of more importance to his welfare and to his recovery from pulmonary tuberculosis than the former. Let every man therefore, in this connexion, beware at all times lest unconsciously he be led by mercenary motives away from that which is truly best for his patient and for the community.

Finally, let me impress upon this meeting of the Therapeutical Section how great has been the influence of sanatoriums in counteracting undue attention to such remedies as drugs and vaccines. The old faith in prescribing and taking some remedy which will exorcise disease from the body dies hard. It would be a pity if present keenness on the administration of tuberculin to consumptives were to bring about any undermining of this influence; for future benefits to the community in the direction of improving bad environment depend

to a considerable extent, in my estimation, upon this influence. The tuberculins must take their proper place in the campaign against tuberculosis.

Dr. Pearson added that with regard to Turban's classification, he did not propose to say whether he thought that was perfect or not, but he did not think it had been done quite justice to that afternoon by the two speakers who referred to it; because they did not seem to have recognized that Turban's classification included a sign indicating whether a patient was febrile or not, and the extent of his fever. In addition to this, if adopted in its completeness, it included simple signs not only indicating whether the lesion was "open" or "closed," but also showing what complicating tuberculous lesion, or secondary organisms, if any, were present.

(The Discussion was adjourned until February 21.)

Therapeutical and Pharmacological Section.

February 21, 1912.

Dr. H. C. CAMERON, Hon. Secretary of the Section, in the Chair.

Discussion on the Uses of Tuberculin in Pulmonary Tuberculosis.¹

DR. J. W. LINNELL: When I was appointed Resident Medical Officer to Mount Vernon Hospital, Hampstead, some two years ago, I was not a believer in the use of tuberculin as a mode of treatment of pulmonary tuberculosis. This unbelief on my part was chiefly due to the fact that I had had no actual experience of its use, and moreover in my very brief experience of the treatment of pulmonary tuberculosis previous to my appointment to Mount Vernon I had been greatly prejudiced against it by the men with whom and for whom I worked; most of these, I need hardly add, had had no actual experience of its use either. However, soon after my appointment as Resident Medical Officer, Dr. Arthur Latham became a member of the visiting staff, and I always look on him as my father in the tuberculin faith. Now after two years' experience, during which time I have treated several hundreds of cases with tuberculin, I would like to say how convinced I am of its value within limits.

If I am asked to give actual proofs of its value, I must reply that I cannot; two years' experience is not long enough; all that I can say is that during that time I have had the opportunity of studying cases lying side by side in hospital, some treated with tuberculin and some treated without tuberculin, and that a slow conviction has settled on me that tuberculin is of very real value in the treatment of pulmonary tuberculosis.

I cannot help thinking that the dispensary workers are as a rule more ready to claim results for tuberculin than we hospital and sanatorium workers; this, I think, may be due to a less perfect knowledge on their part of the course of the disease under ordinary,

¹ Second meeting (adjourned from February 20).

present-day sanatorium conditions; we, who live with our patients, know only too well how all the phenomena of improvement witnessed in a case treated with tuberculin can be matched by like phenomena occurring in a case treated without tuberculin. For example:—

(1) A case is admitted with a certain amount of temperature; this does not show any signs of subsidence under the usual sanatorium methods of treatment—fresh air, absolute rest, &c. After some weeks one determines to try the effect of tuberculin; for some reason or other the administration is postponed; meanwhile the temperature drops, and never rises again while the patient is under treatment.

(2) One comes across a case where the chest seems to dry up in a marvellous manner with tuberculin. It is never very long before one sees a like case where the same phenomena occurs without tuberculin.

(3) To convince an unbeliever, one points out to him a number of one's outpatients, who are working regularly and well, and who are coming up from time to time for injections; he will always be able to point out to you in return a number of his outpatients who have done regular work for many years without tuberculin.

In spite of such facts as these I am personally convinced of the value of tuberculin, and I feel sure that in a few years it will be conclusively proved here in England (as Dr. Inman tells us has been the case in Germany) that there are more real cures and far less breakdowns in patients treated with tuberculin than in patients treated without tuberculin.

Since my appointment to Mount Vernon Hospital I have had the opportunity of meeting workers, not only from all parts of the British Isles, but from America, the Colonies, and the Continent, and I can say with Dr. Latham that up to the present I have never met anyone who has given tuberculin sanely for a year who has not been convinced of its value.

I do not look on tuberculin in any way as a panacea. Speaking generally, in cases where there is any considerable amount of fever, the disease is only aggravated by tuberculin, and naturally tuberculin can do no good in terminal and sub-terminal cases. Such a remark would appear to be absolutely unnecessary, but we in hospitals are constantly having cases in the very last stages of the disease sent in to us as likely to improve with tuberculin treatment. Speaking generally again, the chronic, resistant, afebrile case is almost sure to do well with tuberculin.

If the success of vaccine therapy depends on an ability to make use

of the latent resistance of the individual, it stands to reason that the more resistant the individual, the greater chance of success and vice versa. The chronic, afebrile type of patient has proved that he is resistant; his history often goes back three, four, five years, or even more; his chest is often full of physical signs: never mind; he is in good general health, comparatively speaking; he has put up a good fight, and he will almost certainly do well with tuberculin. This type of case is very much easier to treat than the early case, and I should advise a beginner to start on such a case, unless he can do as Dr. Emery advises and learn tuberculin therapy by treating cases of local tuberculosis where the actual results of injections can be watched from day to day. In cases of early disease, on the other hand, the resistance is an altogether unknown factor and the difficulties are in consequence greatly increased. All one can do is to put such patients on absolute rest under sanatoria conditions, wait till the acute phase (if such be present) subsides, and then start with minute doses of tuberculin, feeling one's way very, very cautiously.

After all is said, however, the only way to know whether a case will do well with tuberculin or not is to try—but to try, I repeat—very, very cautiously. If it is true, as Dr. Latham has said, that every case of consumption that gets well, gets well because of tuberculin, it is also true, speaking broadly, that every case that does not get well, does not get well because of tuberculin. It cannot be urged too strongly that tuberculin is a double-edged weapon. Nevertheless most unlikely looking cases often seem to flourish with tuberculin, and there is certainly a great field for its use in the treatment of chronic cases that have made a good fight and are either only just holding their own, or are slowly going back. In cases of high fever, again, where ordinary sanatorium methods have had no effect, I have occasionally seen what appear to be remarkable results follow the use of very minute doses of tuberculin, but unfortunately such cases seem all too rare.

The more one sees of a disease like consumption, the more one is convinced that the important factor is the patient rather than the bacillus, and in view of the constant succession of physical degenerates who pass before us for examination in the course of our daily work in chest hospitals, one cannot help thinking that the majority are beaten before they come to the starting-post.

Dr. Linnell added that B.E. was much cheaper, and, moreover, put one into line with the rest of the vaccines. He was not acquainted with laboratory matters, but it seemed to him that those who worked

in the laboratory did not quite know what they were doing when they were washing out certain toxins and leaving in others. With regard to the bad effects of B.E., he had only had one case where cold abscesses developed at the site of injection, and this was when he reached big doses of over a milligramme. He had never seen any other ill-effects from using B.E. With reference to method, Dr. Latham had entered very fully into that matter in his address, and it was the method which was adopted at Mount Vernon. He did not think much happened until a reactionary stage was reached, so it was of no use wasting time in a prolonged sub-reactionary stage, although one should at the same time proceed cautiously until a reactionary stage was reached. He had for a long time thought the increase of sputum was a very good rough and ready guide to the presence of a reaction. He was against big reactions, although reactions must be produced in order to know where one was. Of course, one often produced a big reaction without meaning to. He was against big reactions for many reasons. Those who lived with consumptives realized how very ill the patient might be. One was sometimes called to a patient sitting up in bed, breathing like a case of pneumonia, with high fever, severe headache, and the fear of death on his face, and he did not think passing through such a crisis could do the patient any good. There was also the danger that the temperature might not come down again; sometimes this did actually happen. Another factor was the danger of lowering the resistance of the patient against the onslaught of other organisms. He could recall more than one case in which, after a big reaction, the temperature had come down, perhaps for some days, and then there had been a lighting up. He could only attribute this to a lowering of the resistance caused by the reaction being followed by an increased activity on the part of the secondary organisms. However, one could not deny that sometimes after a smart reaction a patient's temperature took on a better phase. The duration of treatment necessary was much longer than he formerly thought; but hospital conditions limited one, and the stress of work and lack of accommodation compelled one to push matters somewhat. With private patients he would go very much slower with the injections. He knew it was not the best treatment to deal with consumptives as outpatients, but what was one to do? He had at the present time under his charge people who had been through hospital and were now attending as outpatients for tuberculin treatment; he had had some of them for eighteen months, and they were going on with their work regularly. It was very important with such people to avoid giving big

reactions. One had only to consider the post-mortem appearance of the lung in a chronic case, and the great amount of caseation, &c., present, to see that the disease could not be healed without a long course of treatment. With regard to laryngeal tuberculosis, about which Dr. Latham had asked him to say a few words, he could only remark in a general way that they had been very favourably impressed by the results which had been obtained in many cases treated with tuberculin at the Mount Vernon Hospital. Mr. Hett was at present engaged in tabulating these results, and it would therefore be premature for him (the speaker) to say anything more about them. But in this connexion it might be of interest to tell people who absolutely denied that the administration of tuberculin by the mouth could cause a reaction, that often in cases of laryngeal tubercle a small dose of tuberculin given orally produced definite reddening of the larynx. He had seen quite a number of such cases. He had not been at all prejudiced, because he had asked Mr. Hett to see them, without having told him anything about the tuberculin; Mr. Hett had then asked him if he knew of any cause for the redness; and he had then told him that the patient had had tuberculin.

In conclusion, he wished to appeal to all believers in tuberculin to be absolutely honest, and not to damn a good cause by misguided enthusiasm. He felt there was a good deal of danger of this happening at the present time. Enough cases had been cured in sanatoria which were not suffering from tuberculosis at all, and he felt many similar cases were now being cured with tuberculin. It was always easy to imagine that the right apex was affected when the old tuberculin reaction was positive. If one claimed to cure such cases, the least one could do was to classify them, and to adopt a severe classification. The cause was a good one and it would be a pity to damn it. Finally, from the worker's point of view tuberculin added greatly to the interest of treatment. It had always seemed to him monotonous work to watch patients rest in the open air, and wait for something to happen: he had done this before he went to work at Mount Vernon. The moral effect of the treatment on the patient was an important factor apart from any physical benefit gained. Many ignorant patients did not think they were having proper treatment unless they were being given medicine, and patients had the greatest faith in tuberculin. Moreover, they were more willing to come and report themselves from time to time; they often travelled quite considerable distances for this purpose and to get their injections, and thus an eye could be kept on them.

Dr. G. A. CRACE-CALVERT said that, so far, the debate had been of a one-sided character, but he could not take the opposite side, as he was a firm believer in the good effects of tuberculin. Still it would have added to the zest of debate if someone had said he could see no more merit in tuberculin than in the ordinary sanatorium treatment of the disease. That seemed to have been the line of criticism of tuberculin. Probably in many cases the difference was not very obvious. But he felt sure that the more one saw of the use of tuberculin in the proper class of case the more one was convinced that it had good effects when judiciously used. It was very difficult to say beforehand whether or not a given case would be benefited by tuberculin. Two cases apparently alike in all respects could be taken and treated by ordinary sanatorium methods: one would make steady progress to recovery, but the other, for no reason which was obvious, might either remain stationary or go steadily downhill. In the same way, one could take two cases apparently alike, and treat one with tuberculin and the other without, and find both were improved, so that it was difficult to say that one did better than the other. He believed many people set off to use tuberculin and expected to get good results at once. He believed it was necessary to experiment somewhat first. One could not say whether a case would react violently or would not react at all; moreover, one could not say that one form of tuberculin would suit it rather than another until a trial had been made. He thought an opinion was often expressed about the substance without it having had a sufficiently extended test, or else the doses were too quickly increased. He had chiefly used T.B.E. He started off with T.R., acting under Sir Almroth Wright; he used that during almost the whole time he was working at the opsonic index, and he believed he got very good results. But he thought the doses were spaced at too long intervals, as one was supposed not to inject while the index was above the normal. Since he had ceased estimating the opsonic index, and inoculated with the physical signs or the general condition as a guide, he had given doses about every three to four days, and he believed the effects had been better. The chief reason he had gone to T.B.E. was that when one used an ordinary vaccine one took the germs just as they were grown, and, after sterilization, so many millions were given. But T.B.E. was made in the same way, and corresponded to the ordinary vaccines, and there might be the same hesitation in using them, if it were not a good thing to use T.B.E., though the T.B.E. was much stronger than ordinary vaccines. He had tried the

bovine bacillary emulsion and P.T.O., but he confessed to disappointment with the bovine tuberculins. With T.B.E. he had not had a bad reaction. With P.T.O. one seemed able to work up to a certain dose, say two or three minims of the second dilution (according to Lucius and Brüning's scale), and nothing would happen. The next stronger dose would then be given, and a huge reaction would ensue. He did not think that could be accounted for by a difference in strength of the dose. He had had that happen in people who apparently stood a dosage to that particular point without any reaction, but a temperature of 103° F. or 104° F., with general malaise and headache, and much local reaction were produced after a next stronger dose, and that condition took two or three days to go down. With T.B.E. there was seldom more than a slight reaction locally. He preferred to get a case of the chronic type for such treatment, but he would be guided chiefly by the physical signs and the general condition, as well as by the patient's behaviour under the trial dose. Naturally one preferred a case in which the disease was quite limited, but if it were fairly quiescent he did not think it mattered much.

In one case in which there was an early lesion of the apex of the right lung, the patient got signs in the apex of the left lung, and extension to the lower lobe on the right side, with the temperature rising. He started him with a minute dose of T.B.E., given in the way recommended by Dr. Hyslop Thompson, of the Liverpool Sanatorium, $\frac{1}{30000}$ mg. in a 6-oz. bottle of normal saline solution, $\frac{1}{2}$ oz. of that being given three times a day half an hour before meals. When that bottle was finished he increased it to $\frac{1}{20000}$, then to $\frac{1}{15000}$, and so on. Eventually he got him on to $\frac{1}{50}$ mg., and the disease all quietened down and he made a good recovery. He had tried another patient in the same way, and although that was only a fortnight ago the physical signs were improved. In some of the acute cases it was worth while trying very minute doses, beginning, with, say, $\frac{1}{100000}$ mg., and not going higher than $\frac{1}{30000}$ mg. He had tried other acute cases with minute doses three times a day but had got no reaction, so the method was not infallible. Unfortunately most sanatorium patients stayed no longer than three to four months, and it was as much as one could do in that time to work up to the required dose. He never started tuberculin in a case until he had watched it on ordinary treatment for a fortnight or longer. Then he proceeded cautiously. He agreed that very good effects were produced with tuberculin given by the mouth, but he preferred to give it

hypodermically, for then it was certain to be all absorbed. He thought it should be given with the patient either in a hospital or in a sanatorium; he did not see how it could be used safely with patients attending the outpatient department of a hospital or dispensary. Every little extra exertion would produce auto-inoculation, and that could scarcely be allowed for in the dosage. He had usually managed to avoid local reaction, and where possible he avoided severe general reaction. It was very uncomfortable to have to treat a patient who had had a severe reaction, for such a patient would sometimes refuse any further treatment with tuberculin. He had one such case now whom he despaired of getting to take it, though he believed it would undoubtedly prove beneficial. Although the tuberculin usually caused an increase of sputum, he had had cases in which for the first day or two it was decreased. He did not know why that should be so, as one would expect an increase. What struck him forcibly soon after he began to use tuberculin was that the number of tubercle bacilli usually diminished considerably. In the sputum of a case when first seen there would perhaps be large numbers of minute scattered bacilli, then after some doses of tuberculin had been given the bacilli were found to be more grouped together—not that they were rapidly dividing, as they seemed larger—and then later on still they were in clumps—i.e., at about the fourth month. One could judge the progress of cases very well in that way by the aspect of the microscopic field. Such a result made one inclined to persist with the tuberculin in the hope of finally getting rid of the tubercle bacilli. The improved character of the sputum came about much more rapidly under tuberculin than with sanatorium treatment alone. He also thought the tuberculin treatment reduced the chance of the patient either reinfecting himself or infecting anybody else, and there was often an improvement in the general condition, especially in increased weight. He also believed that healing of the lung was more rapid under tuberculin, though it was difficult to be certain of that, because two cases might appear to be alike, but were not really so. Another fact, to which he believed Sir James Kingston Fowler was the first to draw attention, was that tuberculin often caused the formation of a cavity in an old case. He believed that to be true, but he did not think it was very serious, because it probably meant that the space which the tuberculin made into a cavity was formerly filled by caseous material, and it was better to have a cavity, only the edges of which were diseased, than a whole solid area of disease. Of course, with a cavity

there was a certain risk from hæmoptysis, but he had only once had hæmoptysis in such a case, and he did not think the risk was very great, as he believed that the cavity resulting from the use of tuberculin was firmer and sounder than that due to the ordinary progress of the disease. Such people he considered more likely to get a firm scar, and less likely to have breaking down. He always made his patients rest half a day before giving the tuberculin, so as to limit the auto-inoculation, while for a whole day afterwards also they should rest.

Dr. A. M. N. PRINGLE joined in the discussion because he had had opportunities of personally carrying out a certain amount of tuberculin treatment, the results of which had been to satisfy him that if cases were carefully selected, and the dosage was equally carefully attended to, excellent results were possible. Of course, one could not expect to cure everything; but if one had an early case and an old case, probably both would do well under tuberculin. There were a number of kinds of tuberculin, but he was impressed by the one fact that it was a question of the interaction of toxins and cells and the production or otherwise of a reaction. Thus it became a matter of the relative value of the toxin and the relative resistance of the cell. So one would use a very small dose of a powerful toxin and a larger dose of a less powerful one. The speaker who got a reaction up to 104° F. with P.T.O. must have been unfortunate, as he had himself used that method for the last eight months, and the highest reaction he had seen was 100·6° F., although he had carried patients up to $\frac{1}{10}$ c.c. P.T.O. The method of giving P.T.O. was that used in Birmingham, and he was sorry the meeting had not heard Dr. Wynn on the subject. He advised those interested in the matter to see what was being done in Birmingham. He entered a strong protest against the attempt now being made to exploit tuberculin as against sanatorium treatment because the former was a cheaper treatment. But it was necessary to bear in mind that the majority of the patients who had to be treated in sanatoria were of the poor class, and that if they were to derive proper benefit from tuberculin they must be placed under the best conditions for the reception of the treatment. Under dispensary conditions the patient would attend once or twice a week for his injection, and the advocates of this system seemed to believe that this would be equal to good food, fresh air, medical control, and all that sanatorium treatment meant. Such a contention was a grotesque absurdity. He had an example of

a man receiving ten shillings a week, with a wife and family to keep. He took him into the sanatorium, and got his dosage up to $\frac{1}{100}$ c.c. P.T.O., and then unfortunately he had to be discharged, and went back to his work. He continued to give the man tuberculin outside the institution, but under the circumstances he could not raise his dose, for the moment he tried to do so there were subsidiary reactions, including headache, palpitation, giddiness, sickness. Later he was able to take him back again. He fed him up and was then able to again get him back to $\frac{1}{100}$ c.c. P.T.O., and on to $\frac{1}{50}$ c.c. P.T., at the present time—a considerable increase. That enforced his point; such patients must be under one's direct personal control; it might be necessary to to rest him, or to give him graduated exercise. He had frequently noticed an increase in the sputum after tuberculin. But the patient under the treatment had an extraordinary sense of well-being when a dose was reached which did good. That he described as the patient's optimum, and naturally that was the temporary maximum. The whole secret of success with tuberculin was finding that point, and then making consistent adequate excursions in the direction of the attainment of a higher degree of resistance. Frequently one found the danger-point was indicated by the occurrence of headache or an unusual degree of local reaction. In order to test that local reaction it was best to go a little below the outer side of the insertion of the deltoid, where a more sensitive point to the tuberculin injection would be found. When there was an unusual needle-track reaction one should hesitate, and temporize by diminishing the dose, or increasing the interval, or repeating a dose of the same strength. If there were unusual general reactions one should wait a week before the next injection, and then one would find probably less reaction and less headache. Then the dose could be increased. The ultimate result would be that, taking sufficient time and care, patients could be brought to the equivalent of 4 c.c. or more P.T.O. by the use of P.T. which clinically is about forty times the strength of P.T.O.; then his practice was to finish the case with O.T. The local and general reaction should be watched, and especially the symptoms which indicated that the patient was having too much. To continue the same doses indefinitely would probably produce hypersensitiveness, and would lead to trouble. He produced hypersensitiveness in one patient and it made him nervous of using tuberculin in that case for some time. But he resumed the injections and went boldly past the point at which he had produced hypersensitiveness before, and now the patient was taking a very large dose of tuberculin indeed.

Dr. CLIVE RIVIERE: I should like to draw attention to a point which has been hardly discussed and is in my opinion too little appreciated, namely, the relation between the small-infrequent-dose and the large-frequent-dose method of treatment. As everyone knows, the small-infrequent-dose method has been mainly practised in this country, where it was introduced by Wright; and the method of "intensive" dosage, as it may be called, is Koch's original method in a somewhat modified form, and has been employed hitherto mainly on the Continent and in America. There has been some natural antagonism between the rival schools in the past, and some tendency on the part of each to doubt the efficacy of the others' method. Indeed, it is only by practice in both methods and a careful study of the literature that a just appreciation of the facts can be obtained. If the literature is studied it is quite obvious that the two methods are successful in a quite different class of case. In Germany and wherever else the large-frequent-dose method is practised we find that phthisis is the disease for which success is claimed and but meagre and uncertain results are obtained in localized tuberculosis. In this country, on the other hand, it is in localized tuberculosis that tuberculin treatment has hitherto found its most striking field of action, while the results in phthisis have been disappointing. Now, at last, as is obvious from the discussion to which we have listened, Koch's method is being reintroduced here, and phthisis is being treated with success. It is amusing to note also, that at the same time in Germany the pediatric physicians are discovering the value of a small-infrequent-dose method in the treatment of tuberculosis in childhood, when it is, as you know, in the main, of a localized nature.

Thus we find the two stages or forms of tuberculosis claim different methods of tuberculin treatment if success is to be achieved. For localized tuberculosis the same small dose repeated at long intervals indefinitely; for autotoxic tuberculosis a gradually rising dosage with the production of tolerance, so that at the end enormous doses can be injected. In the first case we have a process which may be called immunization, consisting in the main of antibody formation and mild focal reactions; in the second we have, added to immunization, tolerance. Tolerance constitutes the sole difference between the results achieved in the two cases.

It has been the fashion for those using the intensive system to smile at the solemn warning of Wright and his followers against the dangers of the prolonged negative phase and its results. It has seemed

impossible to them that doses sometimes a million times smaller than those used by themselves with impunity and advantage could have any action at all—much less a dangerous one. Needless to remark, they were wrong; the minute dose may be equally effective as the large and give rise to similar reaction, providing there is no tolerance to neutralize it. The question is merely one of amount of tuberculous sensitiveness on the one hand (and this varies with amount and activity of disease and other factors), and the presence or not of tolerance to tuberculin on the other hand, whether this is naturally present in autotoxic disease, or is acquired by the injection of tuberculin. Each effective dose of tuberculin is followed by a refractive period, or in other words, a production of tolerance which varies in amount and duration with the effectiveness of the dose. If a sufficient time is waited, say three weeks, in a given case, repetition of the same dose causes the same effect, and this process may be repeated almost indefinitely. This constitutes the small infrequent dose method practised in this country, and no more than the repetition of the same effective dose is needed for the cure of localized tuberculosis.

If, on the other hand, instead of waiting three weeks, we re-inject on the third or fourth day, the refractive period following the first dose has not passed off, and the effect of the second injection is diminished or absent. To make this second injection effective the dose must be raised, and so with tuberculin given at short intervals, the dose must be continually rising if it is to be kept effective. In this way the patient is not only subjected to the immunizing effect of each dose, but at the same time develops a constantly rising tolerance to tuberculin. In cases of autotoxic disease—and this includes nearly all cases of phthisis—this method of giving tuberculin is called for. The small doses of the English school are rendered ineffectual by the auto-tuberculin issuing from the focus of disease; in many cases they are entirely neutralized by a natural formation of tolerance. By the intensive system sensitiveness to tuberculin is gradually overcome, and when large doses are tolerated the patient is in a better position to cope with the poisons of disease, and at the same time auto-tuberculin is less likely to interfere with artificial immunization.

In conclusion, I may say that I find myself very fairly in accord with earlier speakers in this discussion; I would only take exception to Dr. Inman's remarks as to the instability of T.R., as my own experience of this preparation has been very different. I can well believe that P.T.O., to which perhaps Dr. Emery was referring, will rapidly lose its

strength in high dilutions, but T.R. and other endoplasm preparations I should have considered peculiarly stable in this respect.

With regard to the value of tuberculin, I would remark that the value of the small-infrequent-dose method in cases of localized tuberculosis is capable of easy proof, and can hardly be doubted by those who have had real experience. The value of the intensive method, as indeed of all and any remedies in the treatment of a disease like phthisis, is far more difficult of proof. As the result of considerable opportunity in the wards of a chest hospital I have arrived at the personal conclusion that tuberculin, properly administered, is of undoubted value in phthisis; statistics I hold to be quite untrustworthy, for they are practically always vitiated by selection. The strongest evidence in favour of the intensive system of tuberculin administration is its great and increasing spread among the sanatoriums of the world now, more than twenty years after its introduction, and the belief in its value expressed by the highest authorities in those countries where it is most widely used in the treatment of phthisis.

Dr. PAUL MATHEWS (Shrewsbury): In discussing the tuberculin treatment of pulmonary tuberculosis it is obvious that the subject may be approached from many sides and viewed from many aspects. It is more profitable, however, to endeavour to compare the various methods of its employment and assess the value of its results in practice than to indulge in an academic discussion on laboratory experiments. The remarks that follow are based on the observation of some 300 cases treated by tuberculin both in sanatorium and in private practice.

The good results of tuberculin treatment are so well established that it is no longer necessary to discuss whether or not tuberculin should be employed in the treatment of pulmonary tuberculosis, but rather how it should be administered and what are its limitations. The first proposition involves both the question of which preparation to employ and also the method of employing it. The different preparations of tuberculin are so numerous that it is not possible for one observer to assess the relative merits of them all. The observations which follow are, therefore, confined to the use of the various forms of Koch's tuberculin (B.E., T.R., P.T.O., &c.).

In discussing them it is necessary to remember that the specific value of any preparation depends on its ability to excite, in the tissues, the elaboration of an antibody which is specifically antitropic to the active principle of the preparation employed. It is assumed that the

preparation contains the essential proteins and toxins of the *Bacillus tuberculosis*, but the fact that there are so many different preparations of tuberculin shows that it is impossible to preserve unchanged all the proteins present in the tubercle bacilli; for we must assume that the bacilli contain more than one protein, otherwise all the tuberculins would be equally potent or entirely impotent for their specific purpose. In the process of preparation all the essential proteins are not equally preserved, and probably some, at least are altered or destroyed, and consequently each preparation of tuberculin possesses distinctive characteristics according to the mode of its preparation. As an example of the minor differences observed in clinical effects, I have frequently observed that headache, pain in the back, &c., are more frequently caused by an overdose of B.E. than by an excessive dose of T.R., the rise of temperature in each case being similar. The perfect tuberculin has not been prepared and probably never will be. For this reason the value of each preparation is limited, and the suggestion is made that in the rational treatment of pulmonary tuberculosis more than one kind of tuberculin should be employed, and this I am in the habit of carrying out.

The experience of various methods has led me to adopt, as a general routine, the hypodermic injection of Koch's B.E. in rapidly increasing doses at intervals of every three or four days. In uncomplicated cases the initial dose is 0.001 mg. or 0.002 mg., and the dose is increased each time (0.001—0.002—0.003; 0.01—0.02—0.03; 0.1—0.2—0.3, &c.) until a "reaction" occurs. (As a result of experience it is found that it is sufficient to take the temperature at 7 a.m., noon, 4.30 p.m. and 9 p.m.) The dose is then stopped and repeated one week later, or a smaller dose is given (if the reaction has been excessive), and then increasing doses are given as before.

When the dose exceeds 0.1 mg. the injections are made at intervals of a week. In early cases, with patients in good condition, the dosage is increased more rapidly. By this means the patient rapidly tolerates large doses. Not infrequently it is found that patients who tolerate the tuberculin easily up to a certain point are incapable of standing any further increase. In such cases a proportionate dose of some other preparation of tuberculin—e.g., P.T.O.—is administered and the injection continued in increasing doses. If the patient cannot tolerate the initial dose another preparation is tried. When large doses of any one preparation are well tolerated occasional doses of another preparation are employed. In all cases more than one form of tuberculin is used. The

system may be compared to the use of a mixed vaccine or alternative doses of different vaccines in cases of mixed infection (acne, lupus, &c.).

After extensively using the minute doses in vogue a few years ago, and essentially associated with the opsonic methods, I have given them up entirely, and now employ doses of 0.001 mg. up to 5 mg. With these doses I believe progress to be much more rapid and results more certain.

Objections have been raised to the hypodermic method of administration, and it has been sought to prove that oral administration is equally efficacious. My own experience is entirely opposed to this. Admitting that laboratory experiments have shown that a demonstrable effect (as shown by a regular fluctuation of the opsonic index) can follow the oral administration of tuberculin, I still maintain that this method is much too haphazard to be of use in "practice," and that the proportion (if any) of the dose administered that is absorbed is irregular and incalculable, as is shown by the two following instructive cases:—

Case 1.—J. G., male, aged 35, suffering from fibroid phthisis of both lungs. He was given T.R. by mouth daily in doses commencing at 0.00001 mg., subsequently increased to 0.02 mg. three times daily, for two months. During the entire period of administration there was no observable reaction, but at the close of the experiment there was a definite reaction consequent upon a hypodermic injection of 0.02 mg. T.R. Throughout the experiment there was no appreciable change in the pulmonary condition as observed by physical signs and symptoms, but slight improvement in his general condition, probably due to the effect of sanatorium life.

Case 2.—Mrs. D., aged 29. Both apices infiltrated, sub-febrile. This patient had enlarged glands in the neck. She was given T.R. by mouth once a week. The initial dose was 0.002 mg. There was general improvement, but when the patient reached 0.01 mg. the glands began to enlarge and later to soften. She then received three doses of T.R. hypodermically (0.005 mg., 0.01 mg., 0.02 mg.) with the result that the glands rapidly diminished in size and ultimately became firm and fibrous. In this case the inference seems obvious that the orally administered T.R. never had any effect, but there was an immediate response when the administration was hypodermic.

It should be noted that in both these cases the utmost care was taken to ensure that the tuberculin was administered under conditions (as regards the digestive processes, &c.) most favourable to the immediate absorption of the tuberculin unchanged.

For these reasons I am led to conclude that the administration of tuberculin by the mouth leaves too much to chance, and the absorption of tuberculin is thereby too uncertain and haphazard. In practice one constantly finds that a patient's objection to the needle disappears after the third or fourth injection, and there is therefore no good reason for departing from the hypodermic method.

The frequency of the injection depends upon the occurrence or non-occurrence of reactions. If due regard be paid to the temperature, pulse, respiration, &c., the "rapid" method may be safely employed. I consider the estimation of the opsonic method entirely unnecessary in the majority of cases. By exercising due care it is usually possible to increase the doses rapidly without procuring any definite reactions, but at the same time it must be admitted that a brief reaction followed by a rapid return to the normal is usually followed by rapid and more pronounced improvement, both in the general condition and the local lesion.

With regard to the applicability of the method, it may be stated that the majority of cases may be treated by it, though it must be conceded that great caution is necessary when there is mixed infection. At the same time it is certainly not contra-indicated in cases associated with slight pyrexia. Naturally the best results are obtained in Stage I, but the more one uses the method the more one is gratified by the very definite improvement exhibited by patients in Stage II and even Stage III.

Of all the practical advantages conferred by the use of tuberculin, one of the greatest is the fact that treatment can be carried out in the patient's own home, and, provided there is no pyrexia, without interfering with his employment unless that be obviously deleterious. One is repeatedly struck by the very gratifying way in which the patient's occupation continues uninterrupted by treatment. It is of course essential—as in other modes of treatment—that the patient should be freed as far as possible from deleterious and debilitating circumstances, which, by mortgaging his recuperative powers, would handicap the effect of the tuberculin; and the patient should therefore be taught to regulate his life to avoid them. It need scarcely be said that therefore the method should achieve its most notable successes when carried out in a sanatorium, but experience clearly shows that when the patient's circumstances debar this on the score of expenses, &c., the treatment may be carried out at home, and in many cases in Stage I the patient may continue his occupation with every prospect of the desired end being finally, though possibly more slowly, achieved.

A further immense advantage of the method appears in this, that it eliminates the factor which has so often brought discredit on the result of sanatorium treatment—viz., the necessary change in environment. Too often the advantages gained in a sanatorium are rapidly dissipated when the patient returns to his original surroundings. The general improvement which has seemed so striking, and which is so often mistaken by the patient for the index of his condition, too often rapidly passes off and the patient relapses under the influence of his surroundings. The tuberculin treatment introduces no such misleading, transitory and ephemeral improvement. The general condition of the patient improves *pari passu* with the improvement in the local lesion and any appearance of improvement is indicative of a definite gain in the "tuberculin-immunity" of the patient.

Treatment with tuberculin entails no such "return to bad environment" (using the term environment to include climatic, domestic and occupational conditions), but instead a continuance of the same conditions the debilitating influences of which have already been surmounted and to which the patient is accustomed and acclimatized. Three years' experience as superintendent of a sanatorium has convinced me of the importance of not changing the patient's environment for the worse at the close of treatment. This can obviously best be avoided by treating him in the surroundings under which he will continue when treatment is suspended, and this is rendered possible by tuberculin and tuberculin only. These considerations persuade me that the tuberculin treatment is the form of treatment best adapted to the exigencies of general practice, and continued experience of its use only serves to convince me more fully of its wide applicability. By careful manipulation the risks associated with its use become almost negligible, though it is obvious that when such a potent substance as tuberculin is being used the surveillance of the patients must be careful and constant. If proper care be displayed it will be amply rewarded.

Dr. WILLIAM H. WYNN: The cause of recovery from tuberculosis, as from any other infection, is the acquisition of specific immunity. For this two conditions are necessary—adequate stimuli to the production of antibodies, and adequate powers of response upon the part of the organism. Some degree of immunity occurs in every case of chronic pulmonary tuberculosis, as is shown by the fact of chronicity, in spite of the enormous number of tubercle bacilli in the lungs, and by the rarity of general infection, although bacilli continually escape into

the circulation, but when the disease has advanced so far as to be recognized clinically, sufficient immunity for absolute cure is not the rule and the defensive powers need assistance.

We can offer this assistance in two ways—we can increase the power of response and we can control the stimuli. The first is the aim of sanatorium treatment, the second the justification for tuberculin. By sanatorium treatment, by which I mean thorough exposure to the open air, careful regulation of rest and exercise and suitable diet, whether in institutions or at home, we improve the general health of the patient. This is often loosely thought to be equivalent to producing immunity, but it is quite clear to the bacteriologist that the power of resisting infection and the general state of the health are not necessarily associated. Resistance to tuberculosis is a highly specific matter, and an improved circulation, digestion and metabolism do not cause this resistance. It is generally true, however, that the organs concerned in the production of immunity participate in the general well-being of the body and become more capable of responding to stimuli. This is especially so in those febrile cases where the excessive auto-inoculations which had been overtaxing the mechanism of immunity have been prevented by absolute rest and the control of cough.

My conception of the rôle of sanatorium treatment is that it puts the mechanism of immunity in working order; it creates adequate powers of response to immunizing stimuli. This, however, is only one of the conditions necessary for immunity, the other condition, the production of adequate stimuli, is left to chance, and it is here that sanatorium methods alone fail.

We can classify patients into three groups: (1) Those with excessive stimuli which tend to overtax the mechanism of immunity—progressive febrile cases; (2) those with adequate stimuli—improving cases; (3) those with insufficient stimuli—chronic cases with little activity. By absolute rest those in the first class can be transferred to one of the others, cases with adequate stimuli may become cured naturally if the condition can be maintained sufficiently long, but most cases tend to gravitate to Class 3 and become chronic with long periods of inactivity broken by occasional relapses. If we leave the stimuli to chance, it seems to me that what happens is, that in the early stages antigen enters the circulation in abundance, the body responds with antibodies and improvement occurs, but with this improvement the lesion becomes circumscribed and less antigen passes out, and at the same time the antibodies have more difficulty in coming into contact with the bacilli.

The stimuli to immunity, instead of increasing, become less and less and the final result may be arrest but not cure. We have ceased to expect absolute cure from sanatorium treatment, but are content with arrest and the hope that if the immunity can be maintained for sufficiently long cure will at last result. But until the infection is totally eliminated there is always the danger of a recurrence of activity, excessive exercise may force the barriers and cause an auto-inoculation too great for the degree of immunity at the time to cope with, or the immunity may fall below the level of safety by the interference of some intercurrent disease. In this way I have seen the disease become active again fifteen and even twenty years after patients had been sent out of sanatoriums as cured. Professor Fränkel has shown that of 29,029 patients in German sanatoriums who had recovered sufficiently to work again only 897 had lost all their physical signs at the end of five years, that is, 3.09 per cent. were apparently cured.

Has not the time arrived when we should be no longer content to leave the immunizing stimuli to chance, but should aim deliberately at controlling them? We have two methods of doing this—graduated labour and tuberculin. The advocates of graduated labour maintain that it is an advantage to use the patient's own tuberculin in the form of auto-inoculations, and that it is possible to gradually increase the immunizing stimuli by work. I know no proof that it is an advantage to use the patient's own tuberculin; it seems to matter little what the source of the tuberculin is, for patients can be immunized by either bovine or human tuberculin. I am sceptical that by graduated labour it is possible to give increasing doses of tuberculin, for it seems obvious that slight exercise at the beginning of treatment may produce a greater auto-inoculation than severe labour at a later stage, when the disease is circumscribed and quiescent, and I am convinced that to get the highest degree of immunity it is necessary to give progressively increasing stimuli. Graduated labour can only be given in institutions and for short periods, and it has its risks, for in some sanatoriums where it is practised pleurisy and hæmoptysis are more frequent than one would expect. Graduated exercise could as correctly be called graduated rest, and I believe that its results in the arrest of disease, which have not yet been shown to be much superior to those of ordinary sanatorium treatment, are mainly due to the skilful use of rest in the treatment of auto-inoculations.

The great advantages of tuberculin are that a high degree of immunity sufficient for cure can be reached by the skilful use of gradually

increasing doses, that it has a wider scope than any other form of treatment, that in many cases it can be given without institutional treatment, and therefore with a less disturbance of the patient's life and work, and that it is inexpensive. Discussion is mainly concerned with the variety of tuberculin that should be chosen, the best method of using it and the kind of patient most suitable for treatment. The varieties of tuberculin are bewildering, but as my experience has been confined to Koch's tuberculins I shall speak only of these. They may be classified as old and new, bovine and human. It has been supposed that the old tuberculins had mainly an antitoxic action and the new an antibacterial action, but we know very little about the kind of antibodies produced in tuberculosis, and clinically I have found very little difference in the action of the old and new tuberculins and it is possible that the active principle in each is the same. While there is little difference qualitatively there is a considerable difference quantitatively if measured by their power of producing reactions. T.R. is milder than B.E., T.O.A. and P.T.O. than T. or P.T., and P.T. is milder than T. With regard to the choice between human and bovine tuberculins, I think there is an advantage in using bovine tuberculin for pulmonary tuberculosis, at any rate at the beginning of treatment, not for any theoretical reason, but because practically I have found that it is easier to avoid reactions by giving a course of bovine tuberculin before using human. I do this irrespective of the variety of infection which is under treatment.

My views upon the method of treatment have undergone considerable evolution. I first used tuberculin when the work of Sir A. E. Wright brought it again into favour eight years ago. The opsonic index was estimated and small doses of T.R. and later of B.E. were given at comparatively long intervals. Under the influence of opsonic estimations and current teaching my doses became smaller and smaller, and I thought it dangerous to go much beyond $\frac{1}{1000}$ mg. of new tuberculin. I had some success, especially with the milder forms of surgical tuberculosis, but found with pulmonary tuberculosis that while some early cases showed improvement, in most cases a stage was reached when improvement ceased and that in some the treatment could not be continued because of hypersensitiveness. Circumstances compelled me to abandon opsonic estimations and, in spite of my fear of negative phases and reactions, nothing dreadful happened and my results were as before. At the same time I was using vaccines extensively for other infections and found that the best results were obtained by gradually increasing the doses and giving them at shorter intervals. I tried this with tuberculin,

and found that my results were better as the doses became larger and that the best results were obtained in those cases which reached $\frac{1}{2}$ to 1 c.c. of old tuberculin or its equivalent. Attention was then attracted to the work of Spengler, Camac Wilkinson, and others, and I began using bovine preparations. I have no doubt whatever that the results obtainable by the intensive method are immeasurably superior to those obtained by the use of minimal doses. At present I am using the sequence of P.T.O., P.T. and old tuberculin advocated by Camac Wilkinson. I find this sequence convenient, but sometimes use old tuberculin or B.E. for the whole course of treatment. In most cases I begin with P.T.O., a commencing dose being 0.0001 or 0.0002 c.c. Inoculations are given twice a week, the dose being cautiously increased so as to avoid reactions as far as possible, my object being to give the largest dose the patient will stand without a reaction. If a reaction occurs the interval is lengthened and the same dose repeated; it is not often necessary to give a smaller dose and sometimes the interval need not be lengthened. It is often possible to advance to large doses without any reaction. When a dose of 0.2 to 0.5 c.c. P.T.O. is reached P.T. is given; this, while theoretically ten times as strong as P.T.O., is clinically forty or fifty times as strong, so a smaller dose is given. P.T. is taken up to 1 c.c. if possible, but sometimes the limit of tolerance is reached at a lower level, 0.4 or 0.5 c.c. The maximum dose of P.T. is repeated a few times and then a change is made to old tuberculin which, judged by its powers of producing reactions, is ten times as strong as P.T.; so if 1 c.c. P.T. has been given, the next dose is 0.1 c.c. old tuberculin; this is gradually increased to 1 c.c. or even more, and the maximum dose is repeated several times at increasing intervals. Sometimes instead of old tuberculin a final course of B.E. is given. Once tuberculin treatment has begun it is very important that it should not be interrupted, a few weeks' interval may produce hypersensitiveness and considerable difficulty in continuing. It is usually stated that as the doses increase the intervals should be longer, but in many cases I have found it possible to take the patient up to 1 c.c. old tuberculin, with regular inoculations twice a week. It is unwise, I think, to allow a longer interval than ten days even with large doses until the patient has become insensitive to tuberculin. In a few patients I have tried weekly inoculations, but have found that it is more difficult to take the patient up to large doses than with smaller intervals. No definite rules, however, can be laid down, each patient requires individual study, and there seems to be no limit to the experience that can be obtained in giving tuberculin successfully.

The reckless use of tuberculin on its first introduction created an undue fear of tuberculin reactions, and opsonic estimations with their "negative phases" perpetuate it. Occasional reactions do no harm, on the contrary, patients often express themselves as feeling much better after them, but repeated reactions may have a bad effect upon the general health, though not necessarily upon the disease. If a patient shows slight reactions after small doses at the beginning of treatment it is frequently said that the patient is too sensitive and is not suitable for tuberculin treatment. I have given thousands of doses of tuberculin and have never had to stop treatment in its early stages because of sensitiveness. Several patients who showed considerable sensitiveness and frequent reactions have reached doses of more than 0.2 c.c. P.T., but one must admit that it requires considerable pluck on the patient's part to persevere in spite of frequent reactions, and confidence on the doctor's part, a confidence which can only come by using tuberculin on a large scale.

There is an impression that the class of patients suitable for tuberculin is a limited one. On the contrary the contra-indications are few. The great contra-indication is an insufficient power of response to the injections. This is not the same thing as a poor state of the general health; a patient may be in poor general condition and respond very well. The chief cause of a lack of response is a severe mixed infection—the patient with hectic fever and extensive cavitation. A mixed infection *per se* is not a contra-indication, patients with catarrhal complications such as bronchitis, due to other organisms, often do very well by the combined use of vaccines and tuberculin. The tuberculous fever of the early case can be abolished by absolute rest and tuberculin then given. While first stage cases are of course the most suitable for treatment, the most striking improvement is seen in the patients with more extensive disease. Indeed the chronic case with little activity, however extensive the lesions, is generally easier to treat than the early case. Should tuberculin only be given in sanatoriums? If the patient's general condition and powers of response are sufficiently good, there can be no reason why tuberculin should not be given at home, at a dispensary, or a hospital outpatient department. But some patients require preliminary treatment, especially by rest, and if they can receive sanatorium treatment the scope of tuberculin will be enlarged. At Birmingham we have a sanatorium in which patients are kept for six weeks for educational treatment. Whilst there every means is taken to get them into the best possible condition, and as soon as possible

tuberculin treatment is begun. It often happens that every one of the fifty or more patients in the sanatorium is receiving tuberculin. When they leave the sanatorium the tuberculin is continued for as long as possible and in the majority of cases the patients continue at work. Very few of these patients are in the first stage (there is another sanatorium for early cases). At present about 300 doses of tuberculin are given each week. At the General Hospital I treat out-patients with tuberculin and in several instances they have not missed a single day's work. Among my private patients I have treated medical men, nurses, school teachers, clerks, manufacturers, and others, with very little interference with their work. In these cases although the full sanatorium régime is impossible every effort is made to regulate their rest, exercise and diet, and to obtain the maximum amount of fresh air. The best results are obtained by combining with the stimuli of tuberculin measures which promote the powers of response. Open-air treatment and tuberculin are complementary and should not be opposed.

It is sometimes said that tuberculin should be given to the healthy members of a family with a tuberculous history. If a person is *not* infected tuberculin would be useless, as he would be quite insensitive to it, but if an apparently healthy person reacts to tuberculin he is infected, and then tuberculin should be given to get rid of the infection. Tuberculin is then used not for prophylaxis but for treatment.

After an extensive use of tuberculin in every kind of case and under a variety of circumstances, I have reached the conclusion that it is the most valuable remedy we possess in the treatment of pulmonary tuberculosis and that the majority of cases, recognizable clinically, cannot be cured without its use.

Dr. H. CHARLES CAMERON desired to make two observations on the discussion. Dr. Crace-Calvert had deplored the absence of the sceptic in the discussion. That was not the fault of those who were responsible for the organization of the debate. An invitation had been given to several who might have been expected to take up that position, but none had been able to accept it. It was perhaps natural that to appear as the advocate of a new and hopeful remedy should be the more popular rôle. But in a meeting of those who were singularly unanimous and enthusiastic about the use of tuberculin, it should be remembered that there was a great deal of scepticism among men who had had great opportunities for testing the effects of tuberculin. But even if those

agnostics had been present, he doubted whether the meeting would have succeeded in convincing them from the papers which had been read, however ably they might have put forward the position, because of the utter impossibility, as speaker after speaker had declared, of bringing forward statistics, of giving something more tangible than the speaker's own impressions. There was still so much of absolute contradiction, such differences of opinion, not only as to the results of administration, but as to the methods of administration, as to the doses and the period for administration, even as to the object of administration, whether it was to produce a focal reaction or a general reaction, or no reaction at all, that one felt that after the method had been before the profession for twenty years or more some greater degree of unanimity ought to have been attained. The second observation he wished to make was one which was suggested to his mind by what Dr. Vere Pearson had said about the necessity of preventing patients attributing too much of their improvement to the use of tuberculin. Dr. Vere Pearson—and he thought the meeting would agree with him—indicated that sometimes he withheld tuberculin for a time lest the patient should fail to appreciate the importance of other measures of cure, and attribute the whole benefit to tuberculin. On the other hand, Dr. Linnell indicated that he had found benefit from this very tendency, which patients have, to attribute their recovery entirely to the tuberculin; he had used that tendency in outpatient practice to keep his patients together, and to get them to report themselves at regular intervals. Often those who got tuberculin came and those who did not stayed away. Dr. Linnell was in the fortunate position of working gratuitously among the poor. Speakers had put forward the claims for tuberculin so moderately and temperately, that he might be permitted to say that where opinion was so fluctuating, and where in many respects our ignorance was still so profound, we ought to be particularly careful to avoid promising patients more than we felt certain we could achieve.

Therapeutical and Pharmacological Section.

March 19, 1912.

Professor W. E. DIXON, F.R.S., President of the Section, in the Chair.

Ludwig's and other Theories of the Secretion of Urine and the Action of Diuretics.

By Sir LAUDER BRUNTON, Bt., M.D., F.R.S.

DROPSY in patients is always a serious symptom, but it is not the accumulation of water only that is productive of bad results. Accumulation of the waste products of the body is always injurious, and may be fatal, so that their removal is one of the most important problems in therapeutics. The kidneys are by no means the only channel, but they form the most important channel, for the elimination of solid waste as well as of water, and the regulation of their action is most important to the physician. It is almost impossible to understand the diuretic action of medicines unless one has a fairly clear understanding of the mechanism of the secretion in the kidney, and on comparing the accounts of this as given even in recent text-books, it seems to me that a good many of them are imperfect, and that the earlier work on the subject has not received the consideration it ought.

I should not have thought of bringing the subject before the Section to-day had it not been that in looking up a number of recent works I find that there is a good deal of uncertainty in the statements regarding the secretion of urine, and that in the Croonian Lecture of last year, given before the Royal Society, Professor Brodie makes the sweeping statement that all recent work "has proved conclusively that Ludwig's explanation of the glomerular function—viz., that it is a filtering mechanism—is incorrect."¹ A lecture given under such auspices

¹ Croonian Lecture, "A New Conception of the Glomerular Function," by Professor T. G. Brodie, F.R.S. Meeting Abstract of Lecture delivered June 15, 1911.

is very likely to be accepted as possessing undoubted authority, and Ludwig's work is therefore, I fear, likely to be wrongly discredited by it. It may thus be worth while to trace shortly the growth of our knowledge in regard to the urinary secretion.

In a very remarkable paper in the *Philosophical Transactions* of 1842, Bowman¹ showed that the corpuscle or glomerulus, consisting of a tuft of arterial capillaries, was surrounded by a capsule, which formed the commencement of the urinary tubule, so that fluid exuding from this tuft could pass down the tubule and be excreted (loc. cit., p. 74). He further showed that the tubules themselves were surrounded by a capillary plexus, which contained not arterial but venous blood. This venous plexus received blood from two sources, first from the glomeruli, and secondly from the arteriæ rectæ. In this respect the circulation of the kidney resembles that in the liver, where the chief blood supply is derived from the portal vein, but there is also an accessory supply from the hepatic artery (loc. cit., p. 65). On account of this resemblance Bowman gave the name of "the portal system in the kidney" to the venous plexus surrounding the tubules. His idea regarding the secretion of urine was that the proximate principles of the urine were secreted by the tubules from the venous plexus (loc. cit., p. 79) in a more or less solid condition, and were then washed out by water from the glomerulus (loc. cit., p. 76), but instead of stating positively in so many words that this is so, he puts the proposition in the form of a query, "Why is so wonderful an apparatus (as the Malpighian body) placed at the extremity of each uriniferous tube if not to furnish water to aid in separation and solution of the urinous products from the epithelium of the tube?" (Loc. cit., p. 75.) According to Bowman, not only does water pass from the Malpighian bodies, but salts, sugar and albumin, by exudation or transudation (loc. cit., p. 77). He makes no mention of urea, and thus one may infer that he includes this substance in the proximate principles secreted by the tubules, though this is by no means clear, because he speaks of the urinous principles as being sparingly soluble, and was evidently thinking much of urates and uric acid as secreted in serpents. In serpents the urine is solid when passed, and in them the glomerulus and its afferent artery are exceedingly small (fig. 1). But Bowman considered that the urinous principles were in these animals excreted in a more or less solid form by the tubules, and washed out of them by water from the glomerulus,

¹ W. Bowman, *Philosoph. Trans.*, 1842, part i, pp. 57-80.

which, in the case of reptiles, was afterwards re-absorbed in the larger excretory channels so that their urine is solid (*loc. cit.*, p. 79). To put it, then, shortly, Bowman's view consists of four parts: *first*, exudation of water and soluble substances from the glomerulus; *second*, secretion of sparingly soluble urinary constituents, such as urates and uric acid, and possibly of urea by the tubules; *third*, flushing of these constituents down the tubules by water from the glomerulus; and, *fourth*, partial re-absorption of water in the larger excretory channels. Bowman's view was founded entirely upon microscopic examination and he made no experiments.

The subject was again taken up by Ludwig, who modified Bowman's view in two respects: (1) he considered that the whole of the urinary

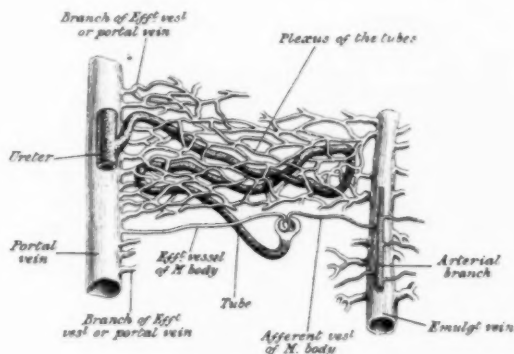


FIG. 1.

Circulation in the kidney of a boa showing the smallness of the glomerular artery. (After Bowman.)

constituents were excreted in very dilute form by the glomeruli, and (2) that selective absorption rather than excretion occurred in the tubules, so that the urine, as it passed through them, became more concentrated, and the relative proportions of soluble ingredients might be altered. His most important work, however, really was the discovery which he made of the relationship between the pressure of blood in the glomeruli and the amount of urinary secretion. By a number of experiments which he made with his pupils Goll and Max Hermann he showed that, other things being alike, the amount of urine secreted depended upon the difference in pressure between the blood in the

glomeruli and the urine in the tubules. When the blood-pressure in the glomeruli was increased the quantity of urine secreted rose; when the blood-pressure was lowered the urine diminished, and when the blood-pressure fell below 40 mm. of mercury the secretion ceased entirely. In his lectures on the secretion of urine, which I attended in the summer of 1869, Ludwig mentioned that by compressing the

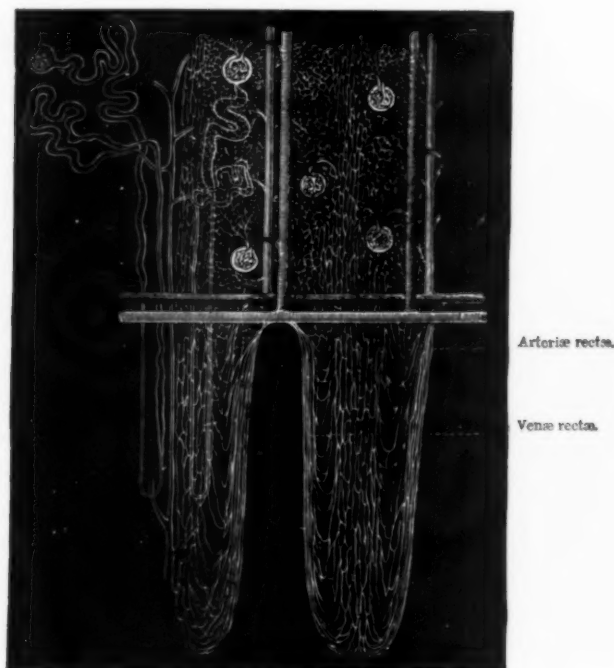


FIG. 2.

Diagram of the tubules and vascular supply of the kidney. On the left is a tubule alone showing Bowman's capsule, the proximal and distal parts of the tubule, connected by the long and narrow loop of Henle, and the collecting tubule. In the middle is a tubule along with the blood-vessels, and on the right are blood-vessels only.

renal artery with a clamp, its lumen might be lessened to one-half without any alteration whatever occurring in the secretion of the kidney, that when it was lessened from one-half to one-nineteenth the secretion of urine was proportionately diminished, and when reduced to less than

one-nineteenth the secretion stopped altogether. In the same way, when the pressure of urine inside the tubules was increased by tying the ureter, the urine was lessened as the pressure increased, and when it reached the height of 40 mm. to 60 mm. of mercury secretion ceased altogether. Ludwig's filtration theory received additional support from the discovery by Henle, in 1862, of the long, narrow loops which bear his name (fig. 2). In relation to these loops we might alter Bowman's question in regard to the Malpighian bodies, and say, "Why is so wonderful an apparatus as this long and narrow tube placed between the wide convoluted tubules if not to present resistance, and to aid in the



FIG. 3.

Diagram showing the form of the urinary tubules in different classes of animals, after Hüfner. 1, Fish. 2, Frog. 3, Tortoise. 4, Bird. 5, Mammal. The letters have the same significance in each: a, capsule of the glomerulus; b, convoluted tubule; c, Henle's loop; d, collecting tube. u in 2 indicates the transverse section of the ureter.

absorption of water, or water and salts, from the fluid passing through the tube?" We might expect that if Henle's loops were cut away less absorption of water would take place, and, consequently, the urine would be more abundant and dilute. This is exactly what does occur when the interior of the kidney is removed, as was done by Ribbert, and I think his experiments are a still further confirmation of the truth of Ludwig's theory. The pressure on the glomeruli usually rises or

falls with the pressure in the arterial system generally, but this is not always the case, because Ludwig found in his experiments with Goll that the amount of water secreted by the two kidneys was quite unequal, sometimes one kidney secreting more and sometimes the other. It was evident that the difference must be dependent upon some alteration in the kidney itself, because both the arterial pressure and the composition of the blood going to both kidneys were quite alike. Ludwig was inclined to attribute this to dilatation of the arterioles supplying the glomeruli in the kidney itself, and not to any alteration in the secreting cells. He did not take up the question of whether these vessels were those which supplied the glomerular tufts at the ends of the convoluted tubules or the arteriæ rectæ.

Ludwig's theory found additional support from the observations of Hüfner "On the Comparative Anatomy of the Kidney." In fishes which do not require any apparatus for retention of water in the body the tubules are short and wide, and the resistance to the passage of urine along them is very small (fig. 3). In tortoises no evaporation from the skin can take place, and there is no necessity for the retention of water, so that in them the contracted part of the tubules is very short. In frogs, on the contrary, evaporation takes place freely from the skin, and in them the tubules, and especially the contracted part of them, are very long. His theory also found much support from the experiments which Ludwig did with his pupil, Max Hermann. These experiments showed that when the content of the blood in urinary substances is nearly alike, the amount of urine secreted rises in direct proportion to the difference between the pressure in the glomeruli and in the uriniferous tubules. But this relation only holds good when the composition of the blood is fairly constant, for he found that when an excess of urea or of water was passed through the kidney, the amount of urea increased, although the blood-pressure remained the same. Although these facts were rather against the purely filtration hypothesis, Ludwig allowed his theory to remain unchanged, without taking the subject up further till the winter of 1869-70, when he began another research on the subject with his pupil Ustimovitch, the results of which led him to make a very important modification in his theory of the secretion of urine, which approximated it very much to Bowman's.

I find that even in recent works of physiology this is not mentioned, and therefore I may be excused if I dwell upon this at some length, more especially as I am one of the few survivors of those pupils of Ludwig who witnessed the epoch-making experiment which Ludwig

made in the winter of 1869-70, and which led him to modify his views. The others are, I believe, Ustimovitch, under whose name the experiment was described, Professor Kronecker, of Berne, and Professor Genersich, of Budapest. Ludwig recognized the great importance of the experiment, and made everyone who was working in the laboratory at that time come in batches to see it. Amongst those who witnessed it, but are now dead, were Professor Schweigger-Seidel, who was Ludwig's histological assistant. Others, who afterwards became professors, were G. Hüfner, in Tübingen, H. P. Bowditch, in Harvard, F. Miescher, in Basel, and J. J. Müller, of Zürich. This experiment consisted in dividing the medulla in the neck of a dog, introducing cannulæ into the ureters and injecting urea into the veins. The division of the medulla caused the blood-pressure to fall very greatly and the secretion of the urine stop altogether. When solution of urea was then injected into the veins the secretion of urine commenced anew, though it had entirely ceased before. This experiment caused Ludwig to make an addition to his pressure hypothesis, namely, "that the effect of the pressure depended upon the amount of urinary constituents in the blood, so that a given difference of pressure between the arteries and the ureters only becomes effective when the blood contains a definite amount of urinary constituents. The reason why chloride of sodium, urea, &c., increases the effect of the pressure may either be that the urine secreted through the glomeruli undergoes further changes through the urinary tubules, or that the permeability of the membranes which surround the glomeruli is altered according to the greater or less amount of urinary constituents in the blood. In all probability both of these factors are concerned."

As it is important that no question should arise regarding the correctness of the translation, I think it best to quote the passage verbatim, especially as the original is not always easily accessible: "Allerdings muss nach diesen Versuchen die Druckhypothese einen Zusatz erfahren, den nämlich, dass die Wirksamkeit des Druckes in einer Abhängigkeit stehe von dem Gehalt des Blutes an harnfähigen Stoffen und zwar in der Art, dass eine gegebene Differenz der Spannungen erst bei einem bestimmten Gehalte des Blutes in Harnbestandtheilen wirkungsfähig werden, beziehungsweise um so mehr Harn liefern könne, je grösser die Anhäufung der Harnbestandtheile im Blute geworden sei. Es dürfte ein lohnendes und wie ich glaube nicht unausführliches Unternehmen sein, die Abhängigkeit der beiden Grossen einer genaueren Untersuchung zu unterwerfen. Die Ursache, weshalb

ein grösserer Gehalt des Blutes an Kochsalz, Harnstoff, u.s.w., die Wirksamkeit der zur Verfügung stehenden Druckdifferenz erhöht, kann entweder darin gefunden werden, dass der aus den glomerulis abgesonderte Harn auf seinem Wege durch die Harncanälchen noch weitere Veränderungen erleidet, oder darin, dass die Durchgängigkeit der Häute, welche die glomeruli umgeben, sich ändert, je nachdem in der Blutflüssigkeit mehr oder weniger Harnbestandtheile enthalten sind, wahrscheinlich ist es sogar, dass die beiden angeführten Gründe bei dem Zustandekommen der Erscheinung betheiligt sind. Spätere Untersuchungen müssen hierüber entscheiden."¹

The reason why this very important change in Ludwig's views has passed unnoticed is that it was published under the name of his scholar, Ustimovitch. Ludwig was in the habit for many years of either publishing his researches conjointly with someone else, or publishing them under the name of his pupils alone, in which case the only acknowledgment of Ludwig's work was that it had been done with his assistance, but only those who had the privilege, as I had, of working with Ludwig, knew what this expression meant. As a matter of fact, almost every research published in this way was devised by Ludwig, the experiments were actually made by Ludwig, and the paper was written out in Ludwig's own hand. Excepting for those who have worked in Ludwig's laboratory, or have learned by conversation from those who have done so, this plan of Ludwig's is sometimes confusing. For example, as an instance of this I may mention that in looking up the references relating to this subject I consulted the Royal Society's catalogue of scientific papers in order to find out where Ludwig and Goll, and Ludwig and Max Hermann had published their work, but I found no reference to it under Ludwig's name, but found it under Goll's and Hermann's names only.

If we now compare Ludwig's modified hypothesis of the secretion of urine with that of Bowman, we find that both agree that water and salts are poured out from the glomerulus, and that both consider that re-absorption of water takes place in the kidney itself, but while Bowman looks upon it as occurring in the collecting tubules, and probably only to a limited extent, Ludwig regards it as taking place in the convoluted tubules, and to a very large extent. To the epithelium of the convoluted tubules Bowman assigned an excreting action, while Ludwig considered it to be an entirely absorptive action in his first theory,

¹ Ludwig's Arbeiten, 5te Jahr. 9. 1870, Leipzig, bei S. Hirzel, 1871, p. 217.

although he leaves it undecided in the last, what the alteration of the of the urine may be as it passes through the tubules. In regard to the passage of urine through the glomerulus, there is very little difference in opinion, Ludwig regarding it a simple filtration, while Bowman calls it an exudation. The great point which was settled by Ludwig's researches, was the relationship between the blood-pressure in the glomerulus and the amount of urine secreted, and I think this may be regarded as a definitely established fact. Heidenhain opposed this view, and considered that the amount of urine secreted depends not on the pressure of blood in the glomerulus, but on the rate of blood-flow through it and the secretory activity of the cells covering the vascular tuft. He based this view to a great extent on the fact that ligature of the renal vein stops secretion, though one would think it must raise the glomerular pressure, but he did not take into account that this procedure causes compression of the tubules and raises the counter-pressure in them, as well as alters the composition of the blood in the glomeruli, which will quickly lose its water. At the same time, the arterioles within the kidney itself will be compressed, and the pressure in the glomeruli may really be lessened instead of increased. Moreover, in his paper with Max Hermann, Ludwig¹ had already discussed the question whether the amount of urine secreted by the glomerulus was dependent upon the rapidity of the blood-flow through it, or the pressure of blood within it. He dismissed the former supposition because he found that in his experiments, not only was there no relationship between the diminution of urine and that of the rapidity of the blood-flow, but that the secretion ceased entirely, while the blood was still flowing with considerable rapidity through the kidney. Another fact which was opposed to the idea that the secretion depended upon the rapidity of the blood-stream was that the secretion ceased when the pressure in the tubules reached a certain maximum, although the blood was still flowing rapidly through the kidney. He therefore concluded that it was the pressure and not the rapidity of the blood-stream in the glomeruli which determined the rate of secretion.

It is by no means easy to arrive at a perfectly certain conclusion regarding the mode of secretion of urine, but it seems to me that all experiments on the subject seem to show that Bowman's original theory, that water and salts are passed out by the glomerulus and the urinary constituents by the tubules, is correct so far as it goes. But it

¹ Ludwig and Max Hermann, *Sitzungsber. d. Akad. d. Wissensch. zu Wien*, 1862, xlv, 2 Abt., p. 347.

has been supplemented by Ludwig's idea of re-absorption in the tubules aided by the resistance opposed to the flow through them by Henle's loops, which were unknown to Bowman, and by his discovery, which is of the utmost practical importance, that the rapidity of urinary secretion rises and falls with the pressure of blood in the glomeruli, or, to speak more exactly, in proportion to the difference between it and the pressure in the tubules. Speaking generally, the pressure of blood in the glomeruli rises or falls along with that in the arterial system generally. We can thus understand why a rise in the general blood-pressure is usually accompanied by increased urinary secretion and a fall in blood-pressure by lessened secretion. Exposure to cold, for example, causes contraction of the cutaneous vessels and a rise in blood-pressure; and when writing my thesis on the subject I found on one occasion that on a cold day,

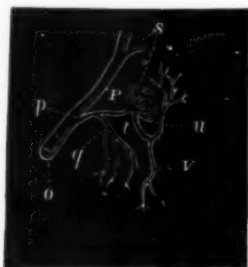


FIG. 4.

Diagrammatic sketch of the vessels in a mammalian kidney. *O* is an artery ascending into the cortical substance of the kidney; *p* is a branch from it which divides into two branches, *q* and *P*; *q* breaks up at once into a number of twigs; *P* is the afferent artery to a glomerulus, *S*, of the lowest row; *t* is the afferent vessel of the glomerulus. It divides into two branches, one of which, *u*, ascends towards the cortex, while the other, *v*, descends towards the medulla. (From Schweigger-Seidel, "Die Nieren," Halle, 1865.)

occurring between two warm ones, the amount of urine I passed was nearly doubled. Warmth has exactly the opposite effect.

Emotion may increase the blood-pressure and the amount of urine. In an observation on myself I found that the excitement consequent on losing a train raised my blood-pressure from 120 mm., which was its normal, to 160 mm., and the effect of excitement in causing diuresis is a matter of everyday observation.

In persons who have a high blood-pressure, either from their normal constitution or from hypertrophied heart or contracted vessels, the secretion of urine is abundant.

When the blood-pressure is normally low, as in weak persons or those suffering from debilitating diseases, or from mitral regurgitation, the secretion of urine is scanty, and in patients who have had a hypertrophied heart with high blood-pressure, the abundant urine begins to be scanty and of higher specific gravity when the heart begins to fail.

But as Ludwig noticed in his experiments with Goll,¹ the kidney contains within itself a mechanism for regulating the secretion of urine quite apart from the general blood-pressure or from the composition of the blood. This mechanism probably resides in the contractile power of the renal arterioles (fig. 4). If these contract greatly they may lessen or completely arrest the secretion of urine, notwithstanding the high blood-pressure, and if they dilate they may increase the supply of blood in the glomeruli and augment the secretion of urine, notwithstanding a fall in the general blood-pressure. It will help us to understand the function of the kidney if we assume, as I think we may perfectly do, that the



FIG. 5.

Diagrams to show the by-pass whereby blood may go to the plexus surrounding the tubules and supply material for excretion of solids without passing through the glomerulus and losing water. (After Meyer and Gottlieb.)

arterioles of the glomeruli may contract while the arteriæ rectæ dilate, and vice versa. If the blood contains much water and the glomerular vessels dilate while those of the arteriæ rectæ contract the whole blood of the kidney will be sent into the glomeruli and free elimination by water will consequently occur. If, on the other hand, it is desirable for the body that water should be retained and waste products excreted this will be effected by the glomerular arteries contracting, when little water will be poured out, while those of the arteriæ rectæ dilate and the venous plexus surrounding the tubules is thus supplied with blood from which the waste products with enough water to keep them in solution are excreted. I discussed this subject more fully than I do now in a paper on "Diuretics" which I wrote in 1884¹ and in my "Pharmacology and

¹ Goll, Henle, und Pflüger, *Zeitschr. f. ration. Med.*, Heidelberg, 1854, iv, pp. 78-100.

² *Practitioner*, 1884, xxxii, pp. 274, 353.

Therapeutics" in 1885, but this does not seem to have received any notice in recent work on this subject, excepting in Meyer and Gottlieb's "Pharmacologie," where it is illustrated by a very instructive diagram which I now reproduce (fig. 5).

One of the most useful of all diuretics is digitalis, and the action of this drug is a complicated one. By stimulating the vasomotor centres it tends to raise the arterial pressure generally, yet it has a special action on the kidney, for Henry Power and I showed¹ that when the secretion of urine was estimated continuously by means of a cannula in the ureter and the blood-pressure recorded by a kymograph, the blood-pressure rose but the secretion of urine diminished or ceased altogether. When the pressure began again to fall the secretion of urine again recommenced, and in some experiments became very copious after the blood-pressure had fallen below the normal. I observed the same, along with Mr. Pye,² in the case of erythrophlœum (fig. 6), and I think that the explanation of it is that both these drugs in large doses may cause such contraction of the renal vessels that the secretion may cease entirely even though the systemic pressure be greatly raised. In our experiments the renal vessels apparently dilated before the systemic, and in therapeutic doses it is quite probable that dilatation of the renal vessels may occur without any previous marked contraction. But in cases of dropsy there is another action of digitalis which I think has not received the attention it deserves. It was shown by Abeles³ and Grützner⁴ that an increase in the proportion of water and of certain soluble substances, such as urea in the blood, causes dilatation of the renal vessels and a more rapid flow of blood through the kidney as well as increased secretion of water. In cases of dropsy, where aqueous fluid is accumulated in the tissues, it is obvious that its absorption into the blood will have the same effect on the kidney as injection of water directly into the veins. Every student is acquainted with Goltz's celebrated "Klopversuch,"⁵ which shows the effect of irritation of the intestine in producing stoppage of the heart and dilatation of the vessels, but another experiment of Goltz's, almost equally interesting, has not received the same attention.⁶ He

¹ *Proc. Roy. Soc.*, 1873-4, xxii, p. 420.

² *Phil. Trans.*, 1877, clxvii, p. 627.

³ Abeles, *Sitzungsber. d. Akad. d. Wissensch. zu Wien*, 1883, lxxvii, Abt. 3, pp. 187-98.

⁴ Grützner, *Pflüger's Archiv*, Bonn, 1871, xi, pp. 370-86.

⁵ Goltz, *Centralbl. f. d. Med. Wiss.*, 1863, p. 593.

⁶ Goltz, *Pflüger's Archiv*, 1871, v, p. 73.

found that if a frog were suspended by the head and the aorta cut across, that at first blood flowed readily from the cut vessel, but if the brain and spinal cord were completely destroyed the flow ceased. If the spinal cord alone were left and saline solution were injected into the dorsal lymph sac, absorption occurred, and fluid again flowed from the cut aorta. Reflex stimulation of the cord caused increased absorption and more rapid outflow from the aorta. So far as I know the experiment has not yet been tried, but we should expect that the addition of digitalis to the fluid in the lymph sac would increase

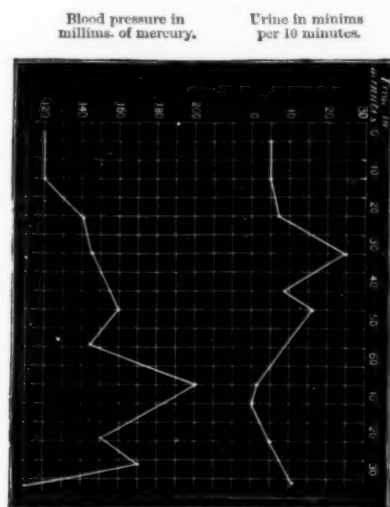


FIG. 6.

Curves showing the effect of erythrophloeum upon the blood-pressure and the secretion of urine. (From *Phil. Trans.*, clxvii.)

absorption in the same way as reflex stimulation, because other experiments have shown that digitalis and its congeners undoubtedly exert a stimulating action on the vasomotor centres in the medulla. An observation of my own made many years ago tends to support this idea, for after taking considerable doses of digitalin I found that my urinary secretion was greatly increased, to such an extent, indeed, that my body seemed to be drained of water and I was forced by excessive thirst to drink more water than my allowance, although for some months previously I had taken every day the same amount of fluid and

the same solid diet without having once exceeded.¹ Digitalis may therefore have not only a stimulating action on the heart and a contracting effect on the vessels of the body generally so that it raises the general blood-pressure, but it may have a special action on the circulation of the kidneys themselves and on the absorption of fluid throughout the body generally. A diuretic action is possessed, too, by substances of the same group as digitalis, but not all of them to the same extent, nor do all the active principles contained in the digitalis leaf have an equal action upon the kidneys.

It is evident that if we can increase the general blood-pressure by digitalis and dilate the vessels of the kidney by combining some other drug with it we will then get most efficient diuresis. Thus Grützner found that nitrate of soda increased secretion of urine both when the blood-pressure was reduced to a minimum by curare and when it was greatly raised above the normal by interference with the respiration. Nitrites may even produce diuresis without any raised blood-pressure, and nitrite of ethyl in the form of nitrous ether has long been recognized as a most useful diuretic, and potassium nitrate has probably a similar though slower action (fig. 7). Another large group of diuretics are urea, the purin bodies, caffeine, theobromine, theophylline, and theocin. These bodies increase the rapidity of the circulation through the kidney, and increase the amount of water poured out through the glomeruli, but at the same time they probably interfere with the re-absorption in the tubuli, as indigo carmine injected along with caffeine does not appear in the epithelium of the tubules as it would do if injected alone. The third group contains the ethereal oils, such as oil of juniper. I do not know that the mode of action of these has been precisely ascertained, but in all probability they act upon the tubules. The fourth division of diuretics is that of salines such as potassium tartrate, and acetate, and also sodium sulphate. According to Meyer and Gottlieb, these salines have an action on the kidney similar to what they have on the intestine, causing secretion in one part and preventing absorption in another. In the kidney they probably increase the exudation of fluid through the glomerulus and prevent its re-absorption in the tubule, or, as Meyer puts it, they cause diarrhoea of the tubules.

Long-continued trial of drugs in cases of disease has shown the advisability of combining different kinds. For example, the *Haustus*

¹ "On Digitalis," &c., reprinted in "Collected Papers on Circulation and Respiration," p. 83.

Diureticus of the fever hospital contains 10 minims of tincture of digitalis, 30 minims of nitrous ether and 40 gr. of acid potassium tartrate, in an ounce of water. The diuretic mixture of St. John's Hospital contains the same ingredients with the addition of vinegar of squill and decoction of broom. The *Haustus Scoparii Compositus* of St. Bartholomew's Hospital contains potassium tartrate, nitrous ether and decoction of broom, whilst a similar one in King's Hospital contains potassium acetate, potassium nitrate, nitrous ether, spirit of juniper and infusion of broom. The effect of the infusion of broom is similar to that of digitalis, the active principle being scoparin. In most of these mixtures we see a combination of drugs which will tend to raise the blood-pressure, dilate the kidney vessels, increase secretion from the tubules, or, like the saline

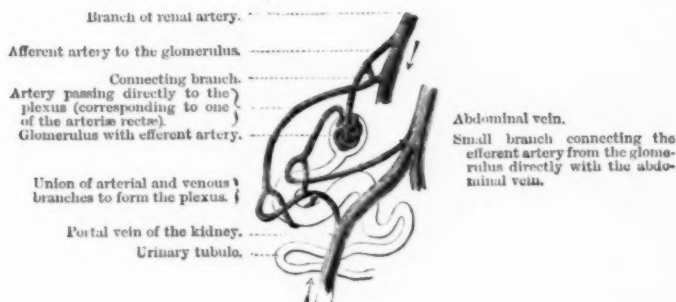


FIG. 7.

Diagram of the circulation in the kidney of the newt. Modified from Nussbaum and arranged to show the parts of the kidney which are probably affected by different diuretics.

diuretics, interfere with re-absorption of water in them. Practical experience has shown physicians what to do, but the rationale of the practice is only now being explained by physiological and pharmacological experiment. Bowman's theory forms the basis of the knowledge we now possess regarding the secretion of urine, but it is Ludwig's experiment on the relation between blood-pressure and secretion that practically enables us to explain the use of diuretics in cardiac disease, and as I have already said, Ludwig's theory, as modified by him in 1870, closely resembles Bowman's though supplemented in some very important respects.

DISCUSSION.

The PRESIDENT (Professor W. E. Dixon, F.R.S.) said he had listened with great pleasure to the paper, which was full of suggestion and historical incident. He was particularly interested to hear what Sir Lauder Brunton said about the vascular condition of the kidney, because so few people appeared to recognize that there were afferent and efferent vessels to the glomerulus, and changes could occur, owing to contraction of either of these sets of vessels, which would bring about differences in the vascular condition of the kidney not usually appreciated. What he meant was that, supposing the efferent vessels from the glomerulus were to become contracted, one would find dilatation of the kidneys as a whole, whereas there would be diminution in the outflow of blood from the renal vein. He was also interested in what the author said about Professor Brodie's Croonian Lecture. Professor Brodie stated that all modern work had tended to show that the kidney was a secretory organ, and not an organ of filtration. He did not know on what evidence that statement was based; in the writings of Professor Brodie and Mr. Barcroft the dictum was laid down that if the kidney was a true secretory organ it must, in producing secretion, do work, and therefore increase the oxygen absorption of the kidney. These observers performed a number of experiments with caffeine, sodium sulphate, and other substances, and showed that when diuresis was produced the amount of oxygen absorbed was increased. But since that time Barcroft and his colleagues had found that Ringer's solution caused an increased secretion of the urine without any increased absorption of oxygen, thus showing, on their own dictum, that the kidney, under those conditions, was not a true secretory organ. It was true that with sodium sulphate diuresis increased absorption of oxygen was observed, but sodium sulphate was a tissue poison; possibly it acted by extracting calcium from the organ, and he had very little doubt that when one diminished the calcium content of an organ, that organ became hyper-active for a time. Much recent work within the last three or four years had shown that. Until it was shown that this increased oxygen absorption by the kidney was specific for the kidney and that other tissues were not influenced in a like way by sodium sulphate, the increased oxygen consumption could not be regarded as in any direct way connected with the diuresis. He (Dr. Dixon) had never worked on the kidney himself, but there were several present who had, and therefore, although Sir Lauder Brunton's paper was full of interest for him, he would prefer to call upon others to discuss it in detail. One remark he would like, however, to add was that the paper left with him a pervading regret that he had not had the privilege of being a worker in Ludwig's laboratory.

Professor CUSHNY, F.R.S., said that he also had listened to the paper with very much interest. Ludwig's theory as generally accepted was based upon his early paper and text-book, which he believed was written before 1869.

He supposed that most of the younger school believed that Ustimovitch was an independent worker as in ordinary laboratories. Those who had been in contact with the paladins of Ludwig's laboratory knew that Ludwig practically wrote everything which came out of it, so that the further development of his theory could be followed through the published contributions of his pupils. In that respect he considered it had been a great loss to physiology and medical science in general that no one had written about the extremely brilliant circle of Ludwig's laboratory. He would remind Sir Lauder Brunton and Professor Kronecker that there were not many left who could speak personally of the circle of workers in that laboratory from 1865 to 1885, and it would be a pious work for those of the older generation, and a work of extreme interest to those who, like himself, had not had the opportunity of working with Ludwig, if some account of that great school could be given. The question of the action of the kidneys was an extremely difficult one, owing to the double vascular supply, and it was very difficult to state how far any one substance acted on the glomerulus or upon the tubules. The view which Sir Lauder referred to in regard to the salines was very inviting, namely, that they caused diuretic diarrhœa, as Meyer put it; but there were some difficulties in the way of that, because the nitrates were not exactly absorbed with difficulty, like the sulphates; and such a thing as urea it was presumably difficult for the tubules to absorb, but it was not difficult for any other cell to absorb. But it might be supposed that the tubules had that specific difficulty in order that they might get rid of urea. With regard to the action of the other diuretics, many of them were very obscure. The digitalis action was full of difficulties, but he thought the idea of Sir Lauder Brunton that possibly digitalis might act as a diuretic by increasing the movement of the fluid in the rest of the body was well worthy of consideration.

Dr. H. H. DALE desired, as one of the younger generation and a newer recruit to pharmacology, to add his testimony to the great interest with which all had listened to the paper, and his appreciation of the privilege of hearing it. He wished to echo Professor Cushny's hope that those records might be put into a more permanent form; that the survivors among English physiologists, such as Sir Lauder Brunton and Dr. Gaskell, who took part in the work of Ludwig's big period, might be able to leave some more detailed record of those days than was at present available. He did not feel competent to offer any criticism in detail of the extremely interesting paper, but wished to ask a question with regard to the alternative route—the so-called by-pass. Sir Lauder seemed to suggest that the kidney might accommodate itself to the needs of the body by a contraction of one or other route, according to whether there was necessity for secretion of water or for the turning out of specific urinary constituents. He wished to know whether Sir Lauder could give any clearer picture as to his conception of the mechanism in which it worked. Whether he considered there was a specific nerve control of the two paths, or the direct action of blood constituents, the different branches of the artery being sensitive to one constituent or the other.

150 Brunton: *Secretion of Urine and Action of Diuretics*

Dr. SIKES said he was glad that Brodie's work had been referred to because he remembered, as a student years ago, feeling confused as to what one ought to say concerning the two opposing theories of renal secretion. Brodie's work had at least made the matter much clearer, especially that part in which he showed the relation existing between the pressure and the amount of urine secreted, and the fact that it did not require very much pressure to bring about quite a large secretion of urine. Brodie's experiments with regard to manometry in the ureter and the estimation of the amount of secretory pressure were of interest.

Dr. H. C. CAMERON mentioned a case of suppression of urine following an operation for excision of one kidney. He was called to see the patient, a middle-aged woman, forty-eight hours after the operation. A gradually increasing drowsiness had ended in complete coma. No urine had been passed since the operation and none could be drawn off by catheter. He injected a solution of urea and within a short time the patient passed urine. Death, however, took place a quarter of an hour later. Examined after death, the remaining kidney showed no evidence of disease to the naked eye. Possibly the action in such a case resembled that in the experiments mentioned by Sir Lauder Brunton. He asked for criticism of the treatment.

Dr. A. J. CLARK said that it had never been his good fortune to do any work on the kidneys, and therefore he could add little to the discussion. He had, however, heard Professor Brodie's Croonian Lecture. He was still unable to understand how the filtration hypothesis explained either Professor Brodie's experiment, in which an increased urinary flow occurred when the pressure in the ureter was raised, or those cases in which urine was passed with a lower osmotic pressure than the blood.

Sir LAUDER BRUNTON, in reply, said the President's observations were of great interest. So far as he remembered, although Barcroft in his first paper held the secretion idea, in his later paper he gave it up and returned to the filtration theory. With regard to Ludwig's work, it might interest many present to know how the experiment he had described was done. It was done by Ludwig and his assistant Salvenmoser, Ludwig always directing and often operating himself, whilst his assistant helped or actually did the operation under his direction, and Ustimovitch stood by with a notebook and recorded what was told him by either Ludwig or Salvenmoser. Afterwards Ustimovitch wrote out a clean copy of the report and gave it to Ludwig, who then wrote the account of the whole thing. The procedure was invented by Ludwig, the experiments were carried out by him or under his direction, and belonged to him. Sometimes he could not do all the experiments, but in every case he did the first two or three, and when the research was well started he allowed his pupil to go on with it. But it was always done on the lines which he had himself laid down, and the apparatus was devised and constructed by him. It would be very interesting to get a list of Ludwig's work, as suggested by Professor Cushny. The only

man who could do it would be Kronecker, and he might possibly undertake it if he (Sir Lauder) asked him to do so. It should be taken on the lines upon which Ludwig worked: (1) on the conditions regulating the pressure of blood in the body and the men who worked at this; (2) the men who worked at the subject of the secretion of urine; (3) those who worked at muscle, liver, lungs and other organs, and the results obtained by investigating the flow of blood through them after death; (4) the men who worked on the heart. He went to Ludwig's laboratory in the summer of 1869, and Coats came a month after he did; Coats's work was Ludwig's entirely. The work he (Sir Lauder) did there on nitrite of amyl were his own experiments, which he did at odd times. The research he was really engaged upon was Ludwig's research on the contractility of the small vessels apart from the central nervous system, and this was put into the paper on amyl nitrite as a preliminary communication. He expected to go back afterwards and finish the work, but he found himself unable to do so. But after he left, Ludwig set Gaskell to work on the same subject, and Gaskell took up Coats's work also and carried that on, with the splendid results which were well known. With regard to this discussion, the mechanism of the double vascular supply could not be easily explained, because different results were obtained according to whether the afferent vessel or the efferent vessel was contracted, or whether the whole of the large arteries going to the glomeruli or the arteriæ rectæ contracted. He did not think it was due to central or peripheral nervous action, but to a local action upon the arterioles themselves by different qualities of blood with which they were supplied. He was unable to be present at Professor Brodie's lecture, and he had not succeeded in getting a full account of it. He thought the work which Brodie did on the kidney had not added very greatly to our knowledge, because all those experiments which had been mentioned with regard to the effect of increased blood-pressure in the kidney and increased pressure from ligaturing the ureter and vein, were to be found in Ludwig's work with Hermann, or with Goll. With regard to the interesting case mentioned by Dr. Cameron, he felt very little doubt that the injection of urea into the vein increased the secretion of urine, and if it had been done earlier it might have had a more happy result. It seemed very much like what one saw in Ustimovitch's experiment, where the secretion of urine had ceased, and where the injection of urea brought it back again. One might try, in addition, cupping over the kidneys, which probably acted reflexly; wet cupping was preferable to dry cupping, if care was taken not to injure the skin thereby. Or one might inject into the intestines some irritant, such as turpentine. He did not know whether this would have had any effect in that case. He had seen extraordinarily good results in apparent coma from it. He remembered a case of pneumonia, in which the patient had some albuminuria and became comatose, and the injection of turpentine into the intestine had a great effect, for the secretion of urine recurred, and the coma disappeared.

Certain Reactions of the Blood in Carcinoma (and other conditions), with Suggestions on Treatment.

By J. A. SHAW-MACKENZIE, M.D.

AMONGST the methods which have been proposed for the treatment of inoperable carcinoma that by means of hypodermic injections of trypsin and preparations of the pancreas has received much attention. The main difficulty in trying this method is the absence of any guide to dosage and of knowledge of the action of such injections on the organism in health and disease. I have experienced the same difficulty in relation to the hypodermic use of certain tissue extracts in malignant tumours in mice. It therefore became evident to me early in the course of my inquiries that if any advance is to be made in this direction, a preliminary investigation of the blood of such animals and patients was necessary, and that the modifications in the blood by the injection of various tissue extracts and substances must be ascertained also, especially in view of the fact that normal serum possesses antitryptic properties.

While my work was in progress the well-known papers of Marcus,¹ Brieger and Trebing² appeared, which stated that the antitryptic power of the blood serum is increased in carcinoma; and the opportunity of prosecuting further work in this direction and on the chemical aspects of the cancer problem was afforded me by Professor Halliburton in the Physiological Laboratory of King's College, London. Whilst working here, Dr. Otto Rosenheim suggested that lipase, the fat-splitting enzyme of the pancreas, should be taken into account also, and since then I have published, partly in conjunction with Dr. Rosenheim, preliminary accounts of the results obtained.³

Contrary to the general idea which prevailed at the time, it was shown that strongly lipoclastic (lipolytic) extracts of the pancreas (pig) can be obtained by the use of glycerin. These extracts retain their activity unimpaired for years. When, however, such extracts are filtered, the filtrate is almost inactive, and the residue left upon the filter

¹ *Berl. klin. Wochenschr.*, 1908, xlv, p. 689.

² *Berl. klin. Wochenschr.*, 1908, xlv, p. 1041.

³ Proceedings of the Physiological Society, February, 1910, *Journ. of Physiol.*, 1910, xl, pp. viii and xii; also *Proc. Roy. Soc. Med.*, 1910, iii (Path. Sect.), p. 168.

paper is also inactive. On mixing together the residue and the filtrate the mixture exerts the same lipoclastic power as the control unfiltered extract. The residue on the filter is destroyed by boiling, but the other constituent of the enzyme, namely, that in the filtrate, is thermostable. This second substance is termed the *co-enzyme* of pancreatic lipase, and the substance in the residue may be spoken of as *inactive lipase*.¹ The chemical nature of the co-enzyme which activates the inactive residue is still uncertain. It was shown, further, that the property which bile salts possess in accelerating the action of pancreatic lipase is shared by many other hæmolytic substances (water, alcohol, sodium oleate, digitonin), and that in all cases this accelerating action is inhibited by cholesterolin, just in the same way that cholesterolin inhibits the hæmolytic action of saponin (Ransom²). We found also that serum, while showing no fat-splitting power of its own, accelerates the activity of pancreatic lipase.³

This power of accelerating lipoclastic activity is greater in the serum of the lower animals than in human serum, but in the serum obtained from cases of carcinoma in man, and in certain other pathological states (diabetes, for instance), the accelerating action is markedly increased; the same increase is seen also in serous effusions in cases of carcinoma; in fact, our first observation was made in a case of recurrent carcinoma of the breast with œdema of the arm. The œdema fluid had no fat-splitting action, but on the addition (made casually) of some of the fluid to pancreatic lipase the great acceleration of its action which ensued was noticed.⁴ Anti-diphtheritic horse serum exerts also an accelerating action.

A similar accelerating influence was found also in non-malignant ascitic fluid from a case of cirrhosis of the liver, but it was absent in the dropsical fluid in a case of heart disease, or at least not greater than is found with normal serum. Various tissue extracts were found to exert also an accelerating influence on pancreatic lipase. In addition to the increased power of accelerating fat-splitting, the serum and serous fluids in carcinoma show increased antitryptic activity, thus confirming the results with serum of Marcus, Brieger and Trebing, already alluded

¹ O. Rosenheim, Proceedings of the Physiological Society, February, 1910, *Journ. of Physiol.*, 1910, xl, p. xiv.

² *Deutsch. med. Wochenschr.*, 1901, xxvii, p. 194.

³ I have ascertained since that H. Pottevin, working with horse serum, found the same thing, *Comptes Rend. Acad. Sci.*, 1903, cxxxvi, p. 767.

⁴ Shaw-Mackenzie and Rosenheim, *Proc. Roy. Soc. Med.*, 1910, iii (Path. Sect.), p. 168.

to, and of Hort¹ and others in this country. In animals, and in the non-malignant cases referred to, which show an increased power of accelerating fat-splitting, the antitryptic power of the serum or fluid is not greater than is found with normal human serum.

My results on mice are more fully described in one of my previously published papers.² Briefly, they are as follows: The same accelerating action of the serum on pancreatic lipase is exhibited in (a) mice inoculated with malignant mouse tumour; (b) mice which proved "negative" to inoculation with mouse tumour; (c) mice which had been inoculated with some of the normal mouse tissues which are known to confer immunity in greater or less degree to subsequent inoculation with mouse tumour; (d) mice which had received subcutaneously injections of similar tissue extracts and substances; and (e) mice which had recovered spontaneously from large growths. I ventured to suggest that lipoclastic acceleration is not a mere accident, but that it may be one factor in the natural defensive or protective processes of the body, and in the induced resistance or immunization to inoculated tumour in mice. At the same time, I alluded to one or two cases of human carcinoma which seemed to support this hypothesis.

I need not go here into details of technique, but I may explain, briefly, that the lipoclastic action is estimated by the amount of decinormal potash required for the neutralization of the fatty acids set free by pancreatic lipase acting on olive oil emulsion, the mixture being incubated at 37° C. for a certain time, usually eighteen hours, phenolphthalein being used as indicator in the titration.

Antitryptic action is investigated by the plate method of previously heated ox serum. A platinum loop drop of standard trypsin solution placed upon the serum plate produces, at 37° C., a depression owing to digestion in a given time. Increasing amounts of the trypsin solution are mixed with a constant quantity of serum, and drops of these mixtures are placed upon the serum plate in the same way. One notes what amount of trypsin is inhibited by the serum, as shown by the absence of digestive effect. One part of normal human serum inhibits four parts of trypsin solution, and the antitryptic value is expressed as 4 to 1.

Substituting hypodermic needle and syringe for bistoury in the old procedure of venesection, 10 c.c. of blood are usually taken.

Since then I have continued my investigation, and I have had now

¹ E. C. Hort, British Medical Association (July), *Brit. Med. Journ.*, 1909, ii, p. 966.

² Proceedings of the Physiological Society, January, 1911, *Journ. of Physiol.*, 1911, xlii, p. xi.

the opportunity of examining the serum in some thirty-four cases of carcinoma. The two reactions, namely, increased fat-splitting acceleration and increased antitryptic action, have been present in all. Similar reactions have been found in two cases of sarcoma examined, and in two cases of rodent ulcer. Confirmation of these results has been obtained in fifteen additional cases of carcinoma, independently examined by Dr. A. W. Sikes, in the Physiological Laboratory of King's College. In some early or doubtful cases, carcinoma has been successfully excluded by the absence of both reactions, and in only two cases have I been uncertain or wrong in my diagnosis.

Coinciding with what I found in spontaneously recovered mice, I have ascertained in four cases that the lipoclastic accelerating power continues in the blood serum after recovery in man. If, therefore, the change in the blood is an indication of an effort of Nature to resist the disease, the serum, so far as lipoclastic acceleration is concerned, continues to remain in this state at least four or five years after recovery under treatment. On the other hand, the antitryptic action returns to the normal or may be subnormal. I append brief notes of these cases:—

Case I: Recurrent Carcinoma of Breast.—The patient came under my observation in March, 1906, and was treated by extracts of the pancreas and intestinal mucous membrane. She improved very greatly, permitting the removal of some supraclavicular carcinomatous and enlarged glands by Mr. P. W. L. Camps, of Teddington, in the following August. Ascertaining in July, 1910, that she was in good health, I asked her to come and see me for the purpose of examining the blood. She readily consented, and 10 c.c. of blood were taken for me by Dr. Vernon Jones. She had no signs of malignant disease, and I understood that she had continued the treatment for some time, and had also been under the care of Dr. T. U. Gray. In July, 1911, I heard that she was suffering from pleuritic effusion of presumed malignant origin. She was then undergoing other treatment, so that I had no opportunity of examining the blood at the time of the presumed recurrence.

Case II: Epithelioma of the Upper Part and Rim of Auricle.—The growth was excised in January, 1903, and some cervical glands were removed in May and December, 1904. In March, 1905, trypsin and ox-gall capsules were prescribed by me and have been continued on and off since. In October, 1911, the patient was in excellent health, without any enlarged glands or recurrence. I then examined the blood, with the result already stated.

Case III: Carcinoma of the Breast.—Operation in 1907. In October, 1911, the patient was in perfect health, and Dr. Mackay, of Lochcarron, under whose care she was, sent me the specimen of her blood.

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Case IV: Inoperable Sarcoma treated by Coley's Fluid.—Under the care of Major Spencer in the Military Hospital, Millbank, in 1906. Recovery was complete, and the case was reported by Major Spencer in the *Journal of the Royal Army Medical Corps*, April, 1909. Major Spencer gave me an opportunity of seeing the patient when undergoing treatment. At that time a large abdominal tumour, which could be felt also *per rectum*, was present. In November, 1911, the patient came to see me, with Major Spencer's permission, for examination of the blood. The patient was in excellent health, and there was no evidence of any growth. I took 10 c.c. of blood; this was examined with the above-mentioned results, which Major Spencer kindly permits me to note.

Recently I have had the opportunity, through the kindness of Professor Hewlett, of examining the blood in a case of recovered early pulmonary tuberculosis, in which tubercle bacilli, formerly present, had disappeared from the sputa. The specimen was taken and forwarded to me by Dr. A. Davies, from a patient at the time in the Dreadnought Hospital. The serum showed a marked lipoclastic accelerating action, and the antitryptic power was normal.

The separation of an inactive pancreatic lipase from its co-enzyme by Dr. Rosenheim has made it possible to analyse the action of serum and other substances on fat-splitting more accurately. The inactive residue obtained by filtration, or by centrifugalizing, can be dried and conveniently kept in a powdered condition. Normal serum activates this residue, but the activation is much more marked with serum from cases of carcinoma, or from those who have recovered from that disease. Tumour extracts exert a marked action also, though they have themselves no fat-splitting power. In the case of tuberculosis just mentioned there was the same action, though it was not so great as in cases of carcinoma. As we do not know at present the nature of the co-enzyme in the pancreatic extract, it is impossible to say whether the activating material in the serum is the same as, or different from, that normally present in pancreatic extracts. Moreover, as already pointed out, the reaction is not specific to carcinoma. By analogy with bacterial infection, without in the least assuming that cancer has a bacteriological origin, it may be permissible to suggest that the activator may be specific in each case, whereas the residue which may be compared roughly to complement is common to all.

The separation of pancreatic lipase into residue and co-enzyme seems to throw an entirely new light on the action of pancreatic preparations in the treatment of carcinoma. I have examined many commercial preparations of trypsin, and amylopsin, and pancreatic

extracts. None has shown any fat-splitting power, but all of them, boiled or unboiled, nevertheless markedly activate the lipase residue.

A similar action is manifested by the serum of mice which had received hypodermic injections of pancreatic extracts and of trypsin; in weak solutions in physiological saline such injections can be given without producing the ulceration which otherwise ensues at the site of the injection, which necessitates the destruction of the animal. Coincident with this action the antitryptic power of the serum rises. If previous to injection the tryptic preparation is boiled and filtered, there is no rise in the antitryptic value of the serum, but its action in reference to lipase is the same as when the unboiled solution is employed.

I was the first to use pancreatic preparations and hypodermic injections of trypsin in the treatment of inoperable cancer.¹ Administered by the mouth in combination with bile salts, I have thought that in certain cases I have obtained beneficial results. It is quite possible, in the light of present knowledge, that such benefit may be due to the co-enzyme of lipase in addition to the accelerating effects on fat-splitting which it is well known are produced by bile salts. The whole subject of the so-called enzyme treatment of malignant disease is, however, at present so obscure that it would be unwise to dogmatize as to which constituent, or constituents, of a pancreatic preparation produces the effect.

Nevertheless, the activating effect of carcinomatous serum on inactive lipase residue is so pronounced, being in fact greater than that of the pancreatic co-enzyme itself, that I have been led, tentatively, to commence treatment in cases of inoperable cancer by subcutaneously injecting the patient's own serum. In five cases, still under treatment, injections of 1 c.c. have been practised at intervals, usually six to eight weeks. Bile salts have been prescribed at the same time, and the blood was examined at the time of each injection. In these cases, and in others where bile salts have been given alone, the action of the serum in reference to lipase remains high or is increased, while the antitryptic action returns to normal and has been maintained at this level for many months. In these cases there has been an improvement in the general and local conditions, but, obviously, it is too early as yet to speak positively on the ultimate value of this mode of treatment. I ascertained later that previous to my commencement Dr. Mackay,²

¹ *Lancet*, 1905, i, p. 386.

² C. G. Mackay, *Brit. Med. Journ.*, 1907, ii, p. 138.

of Lochcarron, had employed similar injections of serum; while treatment with ascitic fluid in carcinomatous cases has been brought forward, from time to time, by observers abroad.

Cholesterin is another substance which has an activating action on the inactive lipase residue, especially in the presence of sodium chloride, with which it forms an emulsion. Cholesterin, however, inhibits the co-enzyme fraction, in conformity with its inhibitory action on accelerators of pancreatic lipase, which I have previously stated. I have fed mice on cholesterin mixed with their food (bread and milk) and in some cases injected it subcutaneously. The serum of such mice activates pancreatic lipase much more than the serum of normal mice does. In the hope that such treatment would exert a curative action I have commenced it recently upon mice with large inoculated growths. In one mouse with a tumour as large as itself cholesterin was added to the food. At the end of four weeks the tumour had entirely disappeared and the animal still remains healthy. In two other animals, selected on account of their large tumours, and treated in the same way, death has occurred owing to adhesions producing obstruction in the bowel, but the tumours appeared to be in a state of complete caseous degeneration. Untreated control mice have died, but no such marked degenerative softening was found in the tumours.

It is impossible to base any positive statement upon so few experiments, but I hope to continue the work and later present evidence of a more decisive kind. Whether treatment on the same lines will prove beneficial in human carcinoma is also a question for the future.

It should be recollected that the late John Holden Webb,¹ of Melbourne, was the first to treat cases of cancer with cholesterin, on the assumption that loss of cholesterin from the living cells was a determining factor in the causation of cancer. Later he abandoned the administration of cholesterin in favour of its solvents, sodium oleate and purified ox-gall. Hofbauer² drew attention also to treatment of tumours by means of cholesterin, while others have noted favourable therapeutic effects of this substance in tuberculosis and other diseases.

Sodium chloride is another substance which has been found to exert a marked activating action on lipase residue, either alone or in aiding the action of other activators.

I have not wished to burden this paper with figures, but it may be interesting to give a few. I have selected those obtained in two cases

¹ *Lancet*, 1901, ii, p. 976.

² *Deutsch. med. Wochenschr.*, 1908, xxxiv, p. 1745.

which are improving under treatment (serum injection); these have the advantage of showing the present condition as compared with that before treatment was commenced; and those obtained in connexion with some experiments on human pancreatic juice.

TABLE I.

Case I.—Inoperable Cancer of Breast.

Before treatment, March 30, 1911, the following figures were obtained:—

(1) 0.7 c.c. of pancreatic extract, diluted with water (1-2), incubated at 37° C. with 2.5 c.c. of olive oil emulsion for eighteen hours and then titrated, required 8.9 c.c. of decinormal potash to neutralize the fatty acids liberated.

(2) The same, plus the addition to extract of 0.5 c.c. of the patient's serum, required 17.5 c.c. of potash solution—an increase of 8.6.

(3) The antitryptic value of the serum was 7 to 1.

The same case after treatment, February 28, 1912. The condition of the patient was quite satisfactory, and the tumour could hardly be felt. The examination of the blood was conducted exactly in the same way as before, and the results were:—

(1) Pancreatic extract alone on olive oil emulsion required 9.4 c.c. of potash solution.

(2) The same, plus the addition to extract of 0.5 c.c. of the patient's serum, required 24.1 c.c. of potash solution—that is, an increase of 14.7.

(3) The antitryptic value of the serum had fallen to 4 to 1.

Case II.—Inoperable Uterine Carcinoma.

The experiments were conducted in exactly the same way. Before treatment, October, 1911:—

(1) Pancreatic extract alone on olive oil emulsion required 11.1 c.c. of potash solution.

(2) The same, plus 0.5 c.c. of the patient's serum, required 21.2 c.c. of potash solution—that is, an increase of 10.1.

(3) The antitryptic value of the serum was 6 to 1.

After treatment, March, 1912: The patient was in good general health, and the local condition reported as satisfactory.

(1) Pancreatic extract alone on olive oil emulsion required 9.4 c.c. of potash solution.

(2) The same, plus 0.5 c.c. of the serum, 23.6 c.c.—that is, an increase of 14.2.

(3) The antitryptic value of the serum had fallen to 3 to 1.

The increase in the lipoclastic acceleration in the foregoing cases, printed above in heavy type (8.6, 14.7, 10.1, 14.2), are much greater than that produced by normal human serum (approximate average 4.5) under the same conditions. In both cases the figure is higher after treatment.

An opportunity has occurred recently in the King's College laboratory of making some observations on fluid obtained from a man who had been operated on for a pancreatic cyst involving the duct, with subsequent

fistula of long standing. The fluid, presumably pancreatic juice (or admixture) by itself, had a very feeble lipoclastic action, but when bile salts, cholesterin, pancreatic co-enzyme, sodium chloride, and serum were added to it the activation was pronounced in each instance; this was especially the case with the serum obtained in the two cases just referred to.

TABLE II.—HUMAN PANCREATIC JUICE OBTAINED FROM A FISTULA.

One cubic centimetre of the fluid was used and 5 c.c. of olive oil emulsion in each experiment, and the mixture kept at 37° C. for eighteen hours. At the end of this time it was titrated with decinormal potash, and the figures given are the number of cubic centimetres of this reagent necessary to neutralize the fatty acids liberated. The substances added to the fluid were as follows:—

	c.c. $\frac{N}{10}$ KOH required
(1) 5 c.c. of water	2.3
(2) 5 c.c. of NaCl solution (0.9 per cent.)	37.2
(3) 5 c.c. of pancreatic co-enzyme	49.3
(4) 1 c.c. of 1 per cent. sodium cholalate + 4 c.c. of water	45.1
" " " " " + 4 c.c. of NaCl solution	50.4
(5) 1 c.c. of cholesterin suspension in water + 4 c.c. of water	17.8
" " " " " emulsion in NaCl solution + 4 c.c. NaCl solution	50.4
(6) 1 c.c. of serum (Case I) + 4 c.c. of water	54.6
" " " " " diluted with water (1.5) boiled and filtered	59.8
(7) 1 c.c. of serum (Case II) + 4 c.c. of water	46.2
" " " " " diluted with water (1.5) boiled and filtered	50.4

Up to the present point I have referred mainly to substances which accelerate or activate lipoclastic action. I shall do no more than mention, briefly, that other substances have the contrary effect. Potassium salts exert an inhibitory action. Working with arsenic preparations, I found that whereas sodium arsenate accelerates, potassium arsenite inhibits fat-splitting. The liquor arsenicalis of the British Pharmacopœia markedly reduces fat-splitting activity, probably in virtue also of the potassium bicarbonate it contains. In this connexion it may be noted that rapidly growing tumours contain a high percentage of potassium in proportion to calcium.¹

SUMMARY.

I have desired in the foregoing paper to place upon record some of the results I have obtained in my work rather than to attempt to draw any sweeping conclusions. In the present stage of the inquiry conclusions of such a nature are obviously impossible. I think, however,

¹ Clowes and Frisbie, "Chemical Pathology," by H. G. Wells, 1907, p. 415.

I may say that up to the present the following points may be considered fairly well proved, or offer suggestions for the future:—

(1) The serum of the blood taken from cases of carcinoma manifests two important properties: (a) an increased antitryptic value; (b) a power to accelerate the action of pancreatic lipase which is far in excess of what is found in normal serum.

(2) These two reactions when present together furnish a valuable aid in the diagnosis of malignant disease, and their absence excludes the diagnosis of cancer.

(3) After recovery or improvement, or during a period of quiescence, the accelerating power of the serum on lipase remains high, or may be even higher than when the disease is manifest. But under the same conditions the antitryptic value falls to normal.

(4) Such reactions serve, therefore, to control treatment and to indicate progress towards recovery or otherwise.

(5) The lipoclastic acceleration is a possible and natural factor in resistance to disease, in carcinoma and in other conditions.

(6) If this suggestion is admitted, serum and substances which increase this action or protective mechanism are indicated in treatment.

(7) Already, although the cases in mice and men are too few to yield decisive results, I have observed a beneficial influence on malignant disease, treated on these lines.

DISCUSSION.

Sir LAUDER BRUNTON said that although he did not feel he could criticize the paper, one or two questions arose in his mind. One was as to whether the blood from which the serum was taken was always at the same stage of digestion. Many years ago he had to do much work with the pancreas, and frequently wanted to get a pancreas from the slaughterhouse. Corvisart was the first to discover that the pancreas in the fasting state had little or no digestive action, but that if one got it during digesting activity the effect was very different. Corvisart said that he got nearly a thousand pancreases from the slaughterhouses in Paris before obtaining a really active one. He (the speaker) found that not only was it during digestion that the pancreas was active—there seemed to be an enzyme liberated which was present only in the form of zymogen in the inactive condition—but he had to pay a man in the slaughterhouse an extra fee, not only for the trouble of getting the pancreas, but for the feeding of the animal before it was slaughtered. The reason given was that they said the flesh of the animal which had been fed shortly before being slaughtered did not eat

nearly so well. This seemed to show that some of the enzyme had been absorbed from the active pancreas. A year or two afterwards he obtained from Kew a papaw plant and found the juice from it much more active than pepsin; it acted in a weakly acid or a weakly alkaline solution, and digested not only ordinary substances but fibrin and connective tissue. He thought it should be a good thing to give, but he was afraid to give it in dyspepsia, because it occurred to him that if the papaw juice was absorbed without undergoing changes in the intestinal wall it might digest the intestinal tissues themselves. It would be interesting to know whether this preparation had been used instead of pancreas in malignant disease.

Dr. H. H. DALE understood the author was treating some of his patients by bleeding them, clotting the blood, and then injecting the serum of that blood into them. Was he not taking from one patient blood at one part and injecting it into another part? If so, it would appear that the curative substance was something which did not exist in the blood as it circulated, but was formed in the course of the changes in the blood outside the body, presumably in the process of clotting, or perhaps in the disintegration of the leucocytes. It was well known that in clotting other changes occurred in blood than the mere formation of fibrin. Years ago it was pointed out by Brodie that a serum, even from the same species, especially when taken quite fresh from the clot, had a very definite physiological and toxic action when injected, even into the animal which it came from. That had been confirmed more recently by other observers, and it had interested him somewhat because the action was of a class which he had been studying recently in connexion with the examination of the action of a certain base derived from the histidine, and resembling the action of extracts from tissues from all parts of the body. This vaso-dilator action was characteristic also of fresh sera. As Dr. Shaw-Mackenzie mentioned that the substance in serum which activated the pancreatic lipase was thermostable, one imagined that it must either be some simple saline substance or some simple body such as the depressant substance formed in the serum by clotting. He asked whether anything had been done, or was being done, towards a further chemical elucidation of the nature of this substance. A thermostable substance which could be dialysed ought to be something which, with sufficient investigation, was at any rate chemically tangible, it should not be altogether beyond the region of investigation. The point raised by Sir Lauder Brunton was interesting in the same connexion. It had been stated by several observers engaged in the preparation of therapeutic sera that it was inadvisable to bleed a horse for the purpose of obtaining therapeutic serum unless the animal had been deprived of food for twenty-four hours previously. Whether that was related to the passage of digestive enzymes into the blood of the digesting animal, or whether it was due to the absorption from the alimentary canal of certain putrefactive products, he did not know, but there seemed to be evidence that the tendency of serum obtained from a horse to produce the incidental effects of serum treatment, rashes, joint pains, &c., was much diminished if the animal was allowed to fast twenty-four hours before the blood was taken.

Dr. SIKES said he did not envy Dr. Shaw-Mackenzie his task of explaining this matter, because it was so technical, and those who had not worked at it would not find it easy to follow. He had seen Dr. Shaw-Mackenzie's work, on which he had been engaged for some years, and a year ago he thought he would try some of the tests for cancer which were described by him. He tried it on twenty or thirty cases, and his conclusion was that there was much in it, as nearly all the cases of cancer turned out according as he had described and the lipolytic and antitryptic reactions were found as he suggested. He had never himself treated any cases, but he had seen many of those which Dr. Shaw-Mackenzie had treated, and could support the fact that there was marked improvement. He recently saw cases which the author had under treatment three years ago, and they were certainly in a very satisfactory condition. The subject was a coming one, and the more that was known about these enzymes or co-enzymes in the blood in carcinomatous conditions the better. What Dr. Shaw-Mackenzie had set out here represented not more than a hundredth part of the work he had done on the subject. The subject was divided into two parts: one was a test for cancer, which came off in practically every case, and the other was method of treating cancer.

Dr. F. PARKES WEBER asked whether any investigations on the same lines had been made in regard to the fluid of peritoneal and pleural effusions in cases of cancer. It occasionally occurred that patients with cancer had chronic peritoneal and pleural effusions obviously directly connected with the primary or metastatic tumours. In such cases, if the fluids obtained by tapping the serous cavities in question were centrifugalized, one sometimes found in the centrifugal deposit a number of flat epithelioid cells (sometimes grouped together in clumps) containing fatty granules in their cytoplasm, and such cells were evidently cancer cells. A good deal had been written in France lately about "auto-sero-therapy," in which method of treatment a fluid derived from peritoneal or other serous effusions had been re-injected into the patient, either subcutaneously or into his veins. In a cancerous case under his care, in which a peritoneal effusion containing cancer cells was tapped once or twice, a secondary growth formed in the abdominal wall in the line of puncture, proving that the peritoneal fluid containing the cells in question could produce secondary growths if re-injected into the patient without preliminary sterilization.

Dr. SHAW-MACKENZIE, in answer to Sir Lauder Brunton, said that he had found variations in normal serum in relation to digestive activity; he therefore usually collected the blood three to four hours after a meal. The glycerin extracts employed were prepared from pig's pancreas; the period of digestion was not ascertained, but extracts made three years ago still retained their full activity. With regard to papayotin or papain, it had been employed by Dr. Branch, of the West Indies, in certain cases of

carcinoma; this observer injected it into tumours (mammary); he (Dr. Shaw-Mackenzie) had been informed by others that when given by the mouth it had been found useful in cases of carcinoma of the stomach. In answer to Dr. Dale on the subject of serum injections, he said that the question of the utility of taking something already in the circulation and putting it back had been raised by others. Dr. Dale had, however, given him the opportunity of comparing the action of blood and serum and he had found that whereas serum had the accelerating action on lipase the blood (unclotted) had not. In the blood the accelerating substance was therefore in a condition in which it was not available for the purpose. With regard to the nature of the accelerating substance, it was pointed out that several materials possess the property, and an investigation on the chemical nature of the pancreatic co-enzyme was at present being carried out at King's College by Dr. Rosenheim and Dr. Myers-Ward. In answer to Dr. Parkes Weber, many examinations had been made with peritoneal carcinomatous fluid, which, boiled or unboiled, reacted like carcinomatous serum on fat-splitting; he had mentioned that such ascitic fluids had been used by observers abroad; the objection to such injections mentioned by Dr. Parkes Weber might be overcome by boiling and filtering the fluid; his own doubt was the question of dosage, and his fear had been the production of anaphylaxis, but he had never noted any indication of this condition in his patients.

Therapeutical and Pharmacological Section.

April 16, 1912.

Professor W. E. DIXON, F.R.S., President of the Section, in the Chair.

The Treatment of Opium Poisoning by the Faradic Current.

By FREDERICK TAYLOR, M.D.

ONE or two experiences in the treatment of poisoning by opium have led me to consider carefully the methods of treatment usually prescribed, and especially the value, mode of application, and time of the application of the faradic current.

The treatment of opium poisoning may be divided into the following parts: the evacuation of the stomach; the use of antidotes; the prevention of a fatal somnolence or coma; and the maintenance of adequate respiration. On the first two heads I propose to say very little. The evacuation of the stomach is obviously desirable, to prevent the absorption of so much of the poison as has not so far been absorbed; it does not touch what is already in the system. But not only in poisoning by opium taken directly into the stomach, but also in poisoning by subcutaneous injection of morphia, lavage of the stomach is desirable, because morphia appears to be eliminated from the system by the stomach mucous membrane, and, it is said, may be reabsorbed and circulate again.

The antidotes commonly employed are atropine injected hypodermically, and dilute solution of permanganate of potassium, of which large quantities are introduced into and removed from the stomach,

while a small quantity is left in. Observations show that the effects of the antidotes are often rather slow in being manifested.

I have rather to consider these cases, or those stages of opium poisoning in which the patient is becoming dangerously comatose, and difficult or impossible to arouse by ordinary measures; in the last phase of which the respiration is reduced to a frequency of 10, 8, or 6 per minute, and becomes irregular and gasping.

Since the chief clinical effect of an overdose of opium is somnolence increasing to coma, which itself may terminate in death by gradual slowing and cessation of respiration, it is natural that efforts should be made to prevent the coma by every possible means; on the understanding, which we have from experience, that a poison like opium, as compared with a structural lesion, is slow in its operation, produces its maximum effects with a rapidity proportionate to the amount absorbed, and gradually loses its influence as a result of elimination. Failing adequate elimination, or neutralization by antidote, the respiratory centre is involved, and death takes place.

Now in spite of the modern method of antidotes there is no doubt that cases occur in which the coma becomes so profound as to call for some other methods of treatment, at any rate, from those who do not like to stand by without any attempt at succour. These methods are, of course, well known to all, but I will repeat them from a text-book much read some years ago—viz., "*Forensic Medicine*," by Dr. W. Guy.¹ After advising the evacuation of the stomach by stomach-pump or emetic he says:—

If the patient is comatose cold water should be freely dashed over the face, head, and neck till he is somewhat roused from the stupor, and he must then be kept awake by causing him to walk rapidly between two assistants, shaking him, and shouting at him. In small apartments, where it is inconvenient to move the patient about, he may be kept roused by flicking the hands and feet with a towel. A current of magneto-electricity passed from the spine through the chest and artificial respiration have been used in extreme cases.

Now no doubt there is an appearance of pure empiricism here, because the treatment by rousing is directed to preventing the onset of a condition which is not in itself fatal; and if it were the fact that opium attacked the respiratory centres and slowed the respiration

¹ 3rd ed., 1868, p. 506.

fatally without first causing complete coma, no amount of keeping awake or rousing would of itself be effective to prevent death. Experience, however, shows that the respiratory difficulty is not pronounced or dangerous until the patient is deeply comatose, and hence the "rousing" method may seem to have its justification. The amount of rousing need only be proportioned to the apparent dose of the poison, but, of course, it can easily be conceived that a dose may be so large as to prevent any response of the cerebral centres to the stimuli applied.

While, however, most writers recommend stimulations of the surface, both directly mechanical and electrical, either for the purpose of rousing the patient from his somnolence, or of exciting his respiratory centres, there are some who regard the whole of this procedure as not only useless but barbarous; and even among the former class the excessive use of stimulation, whether mechanical or electrical, is deprecated on the ground that it may exhaust the strength of the patient.

To some of the objections to external stimulation I should agree, or rather, I accept the objections to some kinds of external stimulation. I think that it is not expedient to walk a patient about who is poisoned by opium, because if the dose is at all large there will inevitably come a time when he will be unable to stand, even though supported by two friends or policemen; and up to this stage he is not really in danger from failure of the respiration. Other stimuli, such as shaking the patient, shouting at him, pinching him, or flicking him with wet towel-ends, or dashing water over his face, are not very efficient, and can, in my opinion, be replaced by the faradic current applied indiscriminately to all the muscles of the trunk or limbs.

The faradic current has been advocated on two grounds: one that it will help to "rouse" the patient by general peripheral stimulation, the other that it will excite the respiratory centre. As a general peripheral stimulant it is directed to be applied to the limbs sharply; by some writers the use of the wire brush electrode is specified as being more directly stimulating to the cutaneous nerves. As to the time at which the faradic current should be used few directions are given. One writer orders it when the patient is somnolent, a condition which is probably implied by other writers when they give no directions at all, since somnolence, less or more, is the chief evidence that the poison which has been taken is beginning to operate. Some writers only refer

to faradism in connexion with failing respiration; and some of these again recommend galvanization of the phrenic nerves, without giving directions as to how it is to be done.

For further information on this subject I have referred to some works on electro-therapeutics. In Dr. Lewis Jones's standard work on this subject¹ I find under the head of "Cardiac Failure" the following:—

The aid of electricity is often invoked for the purpose of resuscitation when death appears to be imminent. It may be applied either in the form of brisk general cutaneous stimulation, as in cases of narcotic poisoning, or with the special object of stimulating respiratory movements or of acting upon the heart itself.

He then goes on to say that application to the cardiac region does not readily affect the movements of the heart, and the results, if obtained, are as likely to do harm as good. For stimulation of the respiratory centres he recommends an induction coil with a long secondary wire, and a metallic brush electrode, applied indifferently to any part of the body, as this method of application is much less likely to produce fatigue or exhaustion than the use of moistened electrodes. He then gives directions for the stimulation of the phrenics in the neck by means of an induction coil with small moist electrodes, and says that it has been successfully carried out in asphyxia and in chloroform poisoning. These general directions may be taken to cover the case of opium poisoning, but this particular contingency is not separately considered.

In an American work on "Electro-therapeutics,"² the author says that paralysis from opium, stramonium, arsenic, &c., is to be treated by general faradization. But I find nothing about the treatment of narcotic poisoning, or of the narcotic effects of opium, or about stimulation of the phrenic nerves.

CASES.

Case I.—My first case occurred more than twenty years ago, when I was called in to see a gentleman, aged 33, who had taken a quantity of

¹ "Medical Electricity," 5th ed., 1906, p. 460.

² Kassabian, Philadelphia, 1907, p. 118.

tincture of opium. He was already in charge of two medical men; he was becoming worse; walking him about had not met with any material success, and he was lapsing into a condition of complete coma. I have no notes as to his pulse or respiration, and am therefore unable to say the exact limit of danger which he reached. But it occurred to me that if exercise of the muscles was a factor in rousing the patient, and possibly in eliminating the poison, a similar result could be obtained by faradizing the muscles and thus getting their frequent and repeated contraction. I procured, therefore, a small Gaiffe faradic battery, which I still have in my possession, and we applied the poles to the muscles of his limbs and trunk indiscriminately with great diligence. After fifteen or twenty minutes the battery became exhausted, and it was recharged with the usual quantity of mercury sulphate. After another similar period it had to be charged again. But during this third dose the patient had become so thoroughly aroused that there appeared to be no fear of his relapsing, and he ultimately recovered completely.

Case II.—My second case is as follows: A gentleman, aged 33, had attacks of abdominal pain for about eighteen months at intervals of three, four, or five months. Each attack lasted from twenty-four to thirty-six hours, and there had been five or six such attacks. A physician had seen him six or seven weeks previously, and said he probably had gall-stone. One evening he went to the theatre, and on his return had some cocoa; he woke up on the following morning with pain in the umbilical region, and some morphia was given. He still had pain the next day, and was frequently vomiting bile. He saw the same physician again on this day, and a gall-stone was again regarded as the cause; but there was no jaundice, and he got a little better. On the following day the abdomen was supple, and painless to manipulation. He referred pain to the lower part of it, and there appeared to be some difficulty in micturition. On the next day again the pain returned; this was again referred to the liver, abdomen, and vesical region, and there was some difficulty in micturition; the flow of urine was twisted or subsided into a dribble; there was no blood with the urine, and it was alkaline. He had some pain in the testes. At 7 p.m. his medical man gave him an injection of morphia to relieve the pain, and I was afterwards sent for to see him. I arrived at the house about 11 p.m., and I spent some time in the dining-room with the medical man hearing

the history and his account of the abdominal symptoms, so that we did not see the patient in his bedroom until 11.20 or 11.25. Directly I got into the room I saw that the patient was in a very serious condition; he was lying low in the bed, was dusky grey in the face, and his breathing was shallow and scarcely perceptible. The pupils were contracted, and he had every appearance of being heavily under the influence of morphia. Later it appeared that the servant had reported at 9 p.m. that "the master looked pinched up like an old man." The medical man stated that he had given him $\frac{1}{4}$ gr., and it certainly struck me that he was curiously vague as to the quantity he had actually given. However, on seeing his condition, I at once pointed it out to the medical man, and we started doing artificial respiration. It was not till 12 p.m. that we got the first independent respiration, but this was not sustained, and on any relaxation of the artificial respiration he stopped breathing again. The pulse throughout was good—such is my note, but I have not recorded its frequency. About 12.15 his muscles resisted a little, his arms became rigid, and his eyelids moved. He breathed spontaneously for a time, but again relapsed. About this time we injected $\frac{1}{50}$ gr. of atropine and in ten minutes another $\frac{1}{50}$ gr. From the first I had suggested the desirability of getting a faradic battery, but it was midnight, the medical man did not possess one, and we were four miles from my house. After a time, however, we succeeded in getting a battery, and at about 12.20 or 12.25 we were able to apply a strong faradic current to the limbs and trunk of the patient. The effect of this was that he was soon roused, but soon again relapsed; he often threw himself over to one side, but at once fell heavily to sleep again. We continued the artificial respiration till 1 a.m. and the battery alone for another quarter of an hour. Finally, at 1.15 a.m., the patient jumped up, got out of bed, and sat on the floor on the far side of the bed, crying out, "I shan't play any longer; what are you doing?"—obviously distressed by the skin and muscle sensations. After this for a time he was wide awake, and only at about 1.40 went off into a sleep, from which he could be easily aroused. The medical man stopped with him for another hour; I left at 2 a.m. Twelve hours later he was well and free from pain; the abdomen was supple, and nothing could be felt in it.

Now I have no doubt that the recovery of these two patients was due to the action of the faradic current in great part, if not entirely.

It is conceivable that by steady persistence in the artificial respiration we might in each case have kept the patient alive sufficiently long for the elimination of the poison, but it is quite obvious that the process was very much hastened by the faradic stimulation.

What is to be noted is, first, that the faradic current was applied to the surface, not by wire brush electrodes, but by small moist electrodes, and this was done with the object of causing muscular contractions, and not merely to stimulate the skin. Secondly, that the stimulations were continued perseveringly, in the first case for at least forty minutes, if not more; in the second case for fifty minutes. Thirdly, that there was not the slightest evidence of any exhaustion as a result of this process. Fourthly, that it had every appearance of directly contributing to the disappearance of the somnolence, and the restoration in the second case of the respiratory functions, although it is true it was preceded by, and continued with, artificial respiration.

It is, of course, interesting to consider whether it acted by *rousing* the patient, at the vagueness of which conception I have already hinted; or by stimulating the respiratory functions; or by hastening the elimination of the poison. It was with this last idea in my mind that I persevered in its use on the first occasion, thinking to myself that the ambulatory process which was always recommended, and which had already been pushed to its limits, possibly acted in that way; not, I must confess, having thought deeply of the mode of elimination of alkaloids in general and of morphia in particular; or, on the other, of the chemistry of muscles and muscular action. From modern works on pharmacology¹ I gather that opium is eliminated principally by the alimentary canal; that it has been found in the saliva, and in the stools of a morphinist; that Alt recovered from the stomach one half of the amount used in a subcutaneous injection; and that it has been detected in the faeces after hypodermic injection. It also passes into the urine, bile, and milk, and perhaps into the sweat. Dr. Dixon, however, says that morphine is entirely excreted by the alimentary canal, and only the merest trace is excreted by the urine²; and later, he says, by the whole alimentary tract.

Its elimination by the stomach renders it expedient that lavage, whether with or without potassium permanganate, should be employed

¹ Whittans, "Manual on Toxicology," 1910, p. 972.

² W. Dixon, "Manual of Pharmacology," 2nd ed., 1908, p. 129.

more than once during treatment, in order to prevent its reabsorption and renewed circulation in the blood; but so far as the alimentary canal beyond the stomach is concerned one must rely upon some potassium permanganate reaching it, or more likely leave it to chance, or to some other antidote, such as atropine.

If strychnine or atropine is taken, it appears that a small quantity is oxidized in the body, but I can find no similar statement with regard to morphia. In any case, it would seem that if muscular contractions have anything to do with the elimination of morphia, it may be by quickening the circulation through that system of the body; but that it is not by any extensive chemical changes, whether of oxidation or otherwise, that the removal of the poison is hastened.

It will naturally be asked whether I recommend this treatment in all cases and all stages. My answer would be that whenever the poison causes a degree of somnolence from which the patient cannot easily be roused, by moderate or determined shaking, the faradic current should be applied to the body and limbs. In proportion to the degree of stupor should be the time during which it should be continued; and when the breathing is slowed and becomes gasping, it should be nevertheless continued and persevered in until the patient is roused and the breathing is restored to the normal, or nearly normal, condition. Artificial respiration should be performed at the same time, but I am sure from what occurred in my second case that the faradic current is a most valuable addition to the procedure, whatever may be its *modus operandi*.

Of course, there is great variety in the severity of the symptoms in cases of opium poisoning, dependent on the amount of opium taken, the time allowed to elapse before the commencement of treatment, and other considerations.

By the kindness of my colleagues at Guy's Hospital I have been enabled to analyse the reports of cases treated at that institution during the last fourteen years, 1898-1911 inclusive. The cases are fifty-five in number, of which all recovered but three. Making a rough estimate as to the degree of severity, I have divided them into three groups: one of cases in which the symptoms were mild and never really threatening, and these formed just over two-fifths of the whole—namely, twenty-three; a second group equal in number in which the symptoms were more pronounced, and recovery was slower; and a third group, in which the symptoms were pronounced or dangerous, numbering nine, or a sixth of the whole. In this last group are, of course, the three fatal cases. Now,

it is interesting to observe that the only cases in which I can find any mention of the use of the battery or faradic current are those three fatal cases. This, of course, might be taken to show that the faradic current did harm, or even killed the patients by exhaustion, but a careful consideration of the cases will, I think, show that this view cannot be held. The real explanation, no doubt, is that the faradic current was only used in the cases which appeared to be of exceptional severity or were not amenable to other means. I will briefly account for them all.

(1) The first case was that of a man aged 24. He was admitted into the clinical ward, and nobody knew whether he had taken any poison or not; but he was said to have had drinks with some friends, and he had fallen in the street two hours before admission. It was said also that a medical man had seen him and injected something into his arm. He came in at 4 a.m. as a dying man, extremely collapsed, cold skin, blue lips, contracted pupils, slow, irregular pulse, and irregular respirations, nine to the minute. He rallied a little with warmth and strychnine, and at 5 a.m., the diagnosis still uncertain, the stomach was washed out and the faradic current was applied about 5.30 and used vigorously for twenty minutes. The effect does not appear to have been marked, but the battery was used several times subsequently. In spite of this he died at 2 p.m. Artificial respiration was used for a short time before his death. An analysis of the stomach contents showed that opium was present; otherwise the organs were healthy.

(2) The second case was admitted into the same ward only a few days later. A man, aged 63, was found unconscious one hour before admission, having in his pocket a 2-oz. bottle, containing a few drops of tincture of opium, the remains, obviously, of a larger quantity. He was admitted into the surgery at 7.15 p.m. profoundly unconscious, insensible to all stimuli, breathing regularly but stertorously, sixteen in the minute. The pulse was full, regular, 80; the pupils very small, not reacting to light; corneal reflex was good; the limbs were quite flaccid. The stomach was washed out with water, and then with solution of potassium permanganate. He made no sign whatever. He was in the ward at 8.15, and a strong faradic current was applied to the face, trunk, and limbs indifferently for a period of at least two and a half hours, and probably longer, by relays of energetic clerks. The pulse began to fail at 9 p.m., Cheyne-Stokes breathing supervened, and he became more cyanosed. Artificial respiration had no effect, but I find no note as to the time at and during which it was used. Half an hour after midnight he died. In addition to the above he had inhalations of oxygen, coffee enemas, and hypodermic injection of 11 minims of liquor strychninæ in divided doses. Post mortem he was found to have fatty degeneration of the heart.

(3) The third patient was a man aged between 40 and 50. He was found in his room in a comatose condition. The medical man first summoned washed out his stomach, and sent him to the hospital. When admitted into the clinical ward he was comatose, with cyanosed face, pin-point pupils, absent reflexes, subnormal temperature, and slow, stertorous, irregular breathing. Three minims of liquor atropinae were injected subcutaneously. He did not respond to slapping with towels, &c., and so he was faradized. To the best of the clerk's memory at the present time, he was faradized for an hour, or an hour and a half, but the report states that after about twenty minutes the breathing was more regular and the corneal reflexes returned. Oxygen inhalation and strychnia by hypodermic injection were administered, and the faradization was stopped. But as the breathing again became worse, and the reflexes weakened, he was again faradized; and this, with a subcutaneous injection of ether and inhalation of oxygen, improved the breathing and the pulse. Subsequently the pulse failed and he died. Morphia was found in the washings from the stomach and in the stomach after death.

In reference to the failure of treatment in these three cases I should offer the following considerations:—

First, that in none of the cases have we any certain knowledge of the quantity of morphia employed; the elderly man who died had a 2-oz. bottle in his pocket containing a few drops of laudanum, and he probably took a large quantity. It must always be conceivable that the quantity of poison may be so large that no measure of neutralization, or of support to the natural powers, while the poison is being eliminated, will be sufficient in the time. In the young man who died it is not clear that the current was used continuously for a very long period, though it was used frequently. We have no note of its effect upon the respiration. The patient was regarded as a dying man on admission, but, for an hour, in consequence of the uncertainty of the diagnosis, no specific treatment for opium poisoning was undertaken. In the last case the faradic current distinctly improved the respiratory function on two occasions; but after the first success it was stopped, and apparently after the second as well.

If the battery is on account of these three cases condemned as useless, so none the less are all the other remedies employed—potassium permanganate, atropine, and stimulations of all kinds.

In this series of hospital cases there were others with a high degree of poisoning in which the patients recovered without the use of the faradic current. In many of these, in spite of the use of potassium permanganate or of atropine, it was not considered safe to leave them

alone without taking stronger measures; but we find such notes as these: "Walked up and down for two hours with short intervals." "Nurse attended to prevent her sleeping; kept awake with great difficulty, walking for an hour or more." "Sleepy; rubbed and slapped; with difficulty kept awake, and later had to be walked about." "Slightly drowsy, walked about for two hours." "Found drowsy, soon unconscious, made to walk up and down for some hours." "Drowsy; friends told off to keep him awake." "Drowsy, falls asleep, constant attention to keep him awake."

I can at present see no reason why, in conditions like this, we should not apply the faradic current to perform the function which constant waking by slapping, or by compelling the patient to perambulate the room, undoubtedly discharges.

The experience of cases shows that the unfavourable condition of somnolence may be increasing some hours after the ingestion of the poison, that it will increase again after temporary amelioration by lavage or "rousing"; and I cannot think it is safe to leave a patient semicomatose until the difficulties of his respiration excite one to perform artificial respiration. I believe that the patient should as soon as possible be roused or awakened, and kept aroused until it is morally certain that the sleep will not pass again into a serious condition of coma. And this I believe can be done by the faradic current, as efficiently, with as little brutality, and as quickly, as it can by any other means.

In cases in which the coma has reached a stage threatening life I think the faradic current should be applied persistently, in spite of the entire want of response during the first thirty or forty minutes, other than the contraction of muscles.

As to the battery employed, I do not think there is any need for an electric current of exceptional strength. My first case was treated by a current from a small Gaiffe battery of which the elements are two zinc plates less than 30 mm. square each, 35 to 40 gr. of mercuric sulphate, and a coil measuring $2\frac{3}{4}$ in. by 1 in.; the whole apparatus can be carried in the coat pocket. The other case was treated by a portable faradic battery, such as is usually employed by the general practitioner.

I have made no lengthy research into the literature of the subject outside manuals and text-books, but remembering the numerous papers on toxicology written by my old teacher, Dr. Alfred Swayne Taylor, I referred to former volumes of the *Guy's Hospital Reports*, and I find

amongst his "Cases and Observations in Medical Jurisprudence"¹ a record, of which the following is an abstract:—

On December 16, 1864, a girl, aged 11½, took at 6.45 p.m. 1½ oz. of laudanum in mistake for black draught. The usual symptoms of opium poisoning rapidly developed, and in spite of washing out the stomach, walking her about, and talking to her, she became quite comatose at 1.30 a.m., the breathing being six to the minute and stertorous. Electro-magnetic shocks were then applied, and roused her so that she was able to take some belladonna, in the form of the extract dissolved in water, and this was repeated by mouth or rectum six times in the next three hours. For some time there was no change, but she gradually improved, the stertor lessening and the breathing becoming more frequent.

The following note is of interest in the present connexion:—

After coma came on, no attempt was made to walk her about, but it was observed that when she had had several electro-magnetic shocks she would make an effort to push herself off the couch and attempt to stand, but immediately relapsed into a profound sleep.

DISCUSSION.

The PRESIDENT (Professor W. E. Dixon, F.R.S.) said the Section was fortunate in having such an authority as Dr. Taylor to give the results of his investigations. In reference to the author's mention of himself, he thought there could be no question now that morphine was almost entirely excreted from the alimentary canal. It was true that formerly the excretion of morphine had been investigated by giving the alkaloid by the mouth and then making examination of the various secretions by all the delicate means known, and this generally resulted in the detection of a small quantity of the alkaloid, but quantitative results were absent. If morphine was administered by the mouth and evidence was clear that it had been absorbed, it was possible to recover about 70 per cent. of that morphine from the faeces. And if one continued to administer the morphine regularly, after a time the secretion of the drug by the faeces gradually diminished, and ultimately a day came when no excretion of morphine by the alimentary canal could be detected. In the case of an animal so treated it was found that if it were killed at this stage morphine was not detected in the body. This was the modern explanation of tolerance—that the body learned gradually to destroy the morphine, in the

¹ Vol. xi, 3rd series, p. 287.

same way as it habitually destroyed bread and butter. It was probably not far wrong, then, to state that in the normal person some morphine was destroyed by the body but the great bulk of it was excreted by the alimentary canal. He felt particularly interested in Dr. Taylor's experiments with the faradic current. He remembered that when he was a student the routine treatment of these cases of acute morphine poisoning was for two unfortunate medical students to take hold of the patient's arms and walk him briskly up and down the ward. His impression had been, in thinking the matter over in recent years, that the beneficial effect of this procedure, if any, might be to keep up the patient's blood-pressure. Sometimes a third student walked behind the patient flicking his skin with a damp towel, the object of this clearly being to excite reflexly the respiratory centre. When the heart was normal in such cases he supposed death occurred from failure of respiration. Therefore if the respiration could be kept going the patient ought to recover. Of all the methods of exciting the medulla, he supposed that the method which Dr. Taylor adopted—namely, powerful faradization of the skin—was the most effectual, and was much better than the administration of a drug like atropine, which at best was but a poor stimulant of the medulla. Probably the faradic current produced its action by exciting the medulla reflexly and producing both a more rapid and deeper respiration.

Dr. A. E. BOYCOTT said he had been wondering whether the efficacy of the faradic current and the other stimuli might not be due to their causing the person to produce more CO_2 . When a person fell into a state of coma the amount of CO_2 in the blood fell, so that the normal stimulus of respiration was reduced. If the stimuli acted in that way, the same result could be brought about by putting dilute acids into the circulation, and he would be interested to know whether this had been tried.

Dr. J. GRAY DUNCANSON did not know of any class of case which called for more courage and resource on the part of the practitioner than that of opium poisoning. The question of faradization brought before one the idea of exhausting the patient, and he had been pleased to hear that Dr. Taylor did not consider that this occurred in his experience. In the cases which he had himself attended he had not tried faradization, but had rather relied upon the hypodermic injection of strychnine, the use of the stomach pump with a very weak solution of permanganate of potash, and what he considered perhaps the most valuable of all measures, artificial respiration. Owing to the stertorous condition of the breathing, the body was already surcharged with CO_2 , and the respiratory centre was long past being stimulated by its presence in the blood; therefore one should try to clear the blood of CO_2 , and keep the respiratory centre going by artificial respiration and the inhalation of oxygen. He had also found great advantage resulting from continual rectal injection of large quantities of saline solution. If it should be his lot to meet with another case

of opium poisoning he would certainly employ faradization on the principles suggested by Dr. Taylor; but he would also retain those other methods which he had found so serviceable in the past.

Dr. WILLCOX said he could confirm the remarks of the President with regard to the excretion of morphia: habitués of morphia, even if the habit had been persisted in for months or years, did not show morphia in their organs. He recently had under his notice two such cases, and failed to find morphia present. Dr. Taylor had done a valuable piece of work in calling attention to the importance of faradism in these cases of opium poisoning. The mode of application of electricity in these instances was scarcely ever paid attention to in the text-books. He would like to know whether Dr. Taylor had tried faradization of the phrenics specially, as well as general faradization. He had generally employed the methods described by Dr. Taylor in cases of opium poisoning, and he had found very useful the methods just mentioned by Dr. Duncanson, especially the giving of salines *per rectum*, which greatly helped the excretion of the poison. In one or two cases of opium poisoning he had known fatal syncope to occur two or three days after the acute symptoms subsided. Two such cases had occurred at St. Mary's Hospital, and he would like to know whether such a thing happened in any of Dr. Taylor's cases.

Dr. CAMERON remarked that, with Dr. Boycott, he would like to find some explanation for the effect of the faradic current in cases of acute opium poisoning other than that of direct stimulation of the medulla. At any rate, the method had not been widely recommended as a means of stimulating an exhausted or irresponsive respiratory centre, as, for example, in atelectasis pulmonum or asphyxia of the newly born. He referred to a severe case of atelectasis in an infant, which after so difficult a labour that the clavicle was fractured, the orbit suffused with blood, and the skull depressed, sank into a drowsy condition with long periods of apnoea, from which it could only be roused by frequent application of cold water to the head and neck. This treatment, continued almost at hourly intervals, was successful in keeping the child alive until respiration was established. He asked whether the faradic current would be likely to be equally successful in such cases.

Dr. OTTO MAY considered it likely that putting an adult into a hot bath and dashing cold water over him alternately might be even more effective than cutaneous stimulation, but obviously the faradic current was much more easy to apply. The essential point was to produce a painful cutaneous stimulation. If the patient were continually pricked with pins it might be effective, but it would be unpleasant because of the bleeding. But with small wire brush electrodes the application of the necessary stimulus by the faradic current was easy, and therefore the most useful way of producing what was required.

Mr. G. W. JOHNSTONE said he thought Dr. Cameron's analogy of the new-born child in a state of asphyxia with a person suffering from opium poisoning

was very interesting. He agreed with those remarks as to the convenience of the faradic current. An important point was that in the case of the new-born, whilst the flicking and the hot and cold douching were being carried out, time was gained, the *vis medicatrix naturæ* came into force, and as hours and days elapsed the child gradually recovered from the injury. In the case of the adult suffering from opium poisoning, in like manner we should not overlook the fact that at least time was gained whilst the gentle process of stimulation by the faradic current was being used.

Dr. A. J. CLARK said he was especially interested in the suggestions which had been made as to the mode of action of the faradic current, and as to the possibility of the destruction of morphia by muscles. The liver could destroy some alkaloids, and the brain might destroy some, but he did not know that the muscles ever had the power to destroy alkaloids. With regard to the question of whether the faradic current acted beneficially by producing excessive CO_2 , he saw one case recently which had a form of periodic breathing consisting of three gasps followed by a period of apnoea, and during the apnoeic period the patient became extremely cyanosed. Oxygen was applied in such a way that the patient was receiving over 90 per cent. of oxygen into the lungs, and that improved the respiration enormously. The patient's general condition also became better. The corneal reflex had been absent for a time. Once the patient even became partly conscious. Unfortunately the faradic current was not tried, and the patient ultimately died. He did not doubt, however, that the oxygen greatly improved the condition, and that if the kidneys and arteries had been healthy he would have survived. This case suggested that excess of CO_2 had an injurious action, but that excess of oxygen had a beneficial action. This idea was borne out by the blood-pressure and pulse-rate. The case did not show typical Cheyne-Stokes respiration.

Dr. FREDERICK TAYLOR, in reply, expressed his satisfaction at the discussion which his paper had aroused. His chief point was to ascertain in what way the faradic current acted. His idea in applying it had not been to stimulate the respiratory centres, and he was not sure whether his two patients suffered more from skin sensation or from muscle sensation. His intention had been to act through the muscles. With regard to the remarks of the President on elimination, it was very interesting to realize that the morphia gradually came to be tolerated in the body, and the system got into the habit of practically destroying the poison. But it would be admitted that this did not happen in acute cases; and there it must act prejudicially. With regard to the action of the faradic current and the respiratory processes, as he said in the paper, his feeling was that the patient must be roused and prevented from getting into such a condition that the respiratory centre failed. That required an analysis of the processes of somnolence and asphyxia which he had not yet worked out. He had yet to know what was the exact link between the somnolence and the failure of the respiratory centres; but apparently if one

prevented the somnolence the asphyxia also was checked. The faradic current seemed to him much better than knocking the patient about or flicking him with towels. He had not in these two cases attempted to faradize or galvanize the phrenics; indeed, faradization of the body generally had so far satisfied him that he had no need to experiment on the phrenics. With regard to Dr. Willcox's question about fatal syncope, he did not remember to have seen a case of the kind; and in the case at Guy's Hospital, the records of which he had looked up, there was no note of such an occurrence. In the three fatal cases the patients died apparently in a state of coma and asphyxia. The President suggested that the original idea of general stimulation of the muscles by walking about or otherwise was to increase the blood-pressure. Dr. Taylor would have thought that the routine treatment of opium poisoning was long antecedent to modern conceptions of blood-pressure. It seemed to him that increased rapidity of the circulation might help elimination.

Therapeutical and Pharmacological Section.

June 4, 1912.

Professor W. E. DIXON, F.R.S., President of the Section, in the Chair.

The Influence of Ions upon the Action of Digitalis.

By A. J. CLARK, M.B.¹

IN the experiments described below I have studied the action of the digitalis glucosides upon the isolated frog's heart, and have endeavoured to ascertain to what extent this action is modified when the composition of the perfusion fluid is altered.

(I) METHOD.

The method was one described by Hartung [2]; I have modified it slightly (fig. 1). As shown in the figure, a cannula connected with a small reservoir is ligatured into the sinus venosus of the frog, a second cannula, connected with a short piece of bent tubing, is inserted into one aorta, the other aorta is ligatured, the superior venæ cavæ are ligatured, the frog's heart is cut free from the body, and the apparatus is fixed on to a piece of cork with pins, being so arranged that the fluid circulates freely. By varying the size of the reservoir any quantity of fluid from $\frac{1}{2}$ c.c. to 10 c.c. can be circulated through the heart for any length of time desired, the pressure remains constant, and the circulation of the fluid provides aeration, rendering oxygen unnecessary. The movements of the heart are recorded by a light lever on a smoked drum. By means of the two T-tubes and clips, shown in the figure,

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the cannula can be washed out without altering the pressure. In the experiments described below the diastolic pressure was always about 4 cm., and the systolic pressure 5 cm. of water; the temperature varied between 12° C. and 16° C.; Ringer's fluid of the following composition was used—NaCl 0.65 per cent., KCl 0.018 per cent., CaCl_2 0.024 per cent., NaHCO_3 0.02 per cent. In this medium a frog's heart maintained a strong, steady beat for twenty-four hours, without the addition of glucose or the passage of oxygen. Most of the experiments were performed with crystalline digitoxin, kindly supplied by Messrs. Merck

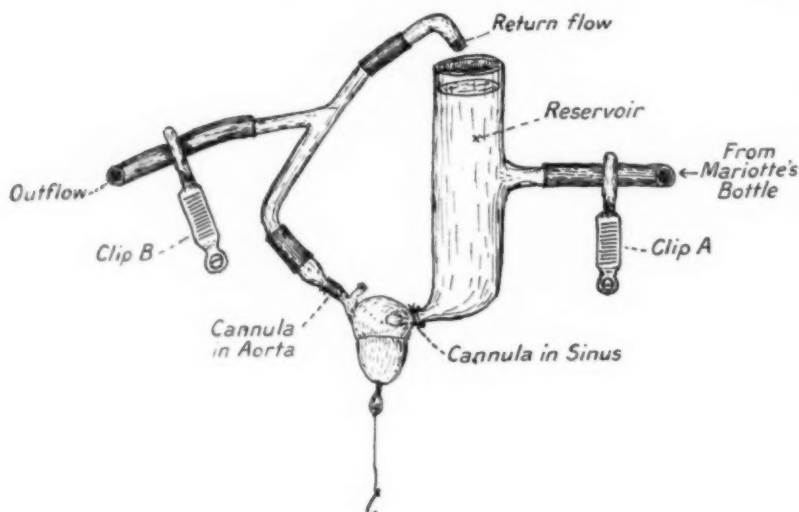


FIG. 1.

Apparatus for perfusion of isolated frog's heart. (Natural size.)

and Co. A few experiments were performed with strophanthin (commercial preparation from *Strophanthus hispidus*—Burroughs Wellcome and Co.). The drug was dissolved in alcohol (1 mgrm. per cubic centimetre), and stock solutions kept in this form. It was proved by experiment that the solutions in alcohol suffered no loss of strength on keeping, but dilute solutions of digitoxin in Ringer's fluid showed a marked loss of activity after twenty-four hours, therefore freshly made solutions were always employed.

(II) THE EFFECT OF CONCENTRATION UPON THE ACTION OF DIGITOXIN AND STROPHANTHIN.

Schmiedeberg [6], Krailsheimer [5], Holste [4], and Werschinin [9] investigated the action of these drugs, using Williams's apparatus, in which 50 c.c. of fluid are perfused through the heart, which works under a diastolic pressure of over 10 cm. of water. Trendelenburg [8], Straub [7], and Heffter and Sachs [3] did similar experiments, using Straub's apparatus, in which 1 c.c. or 2 c.c. of fluid are used and the diastolic pressure is only 2 to 3 cm. of water. Werschinin and Straub obtained the following results:—

TABLE I.

Observer	Drug used	Minimal concentration of drug in milligrammes per cubic centimetre producing systolic arrest
Werschinin ...	Gratus strophanthin (Thoms) ...	0.01
	Amorphous strophanthin (Böhringer) ...	0.001
	Digitoxin cryst. (Merck) ...	0.01
Straub	Gratus strophanthin cryst. (Merck) ...	0.0025 to 0.00125

From these results it appears that gratus strophanthin and digitoxin are of nearly the same strength, but that amorphous strophanthin is many times more toxic. It will also be seen that with Straub's apparatus much lower concentrations of gratus strophanthin produce systolic arrest than produced systolic arrest with Williams's apparatus. Straub found that if $\frac{1}{2}$ c.c. of fluid were used instead of 1 c.c. the same concentration of strophanthin still produced exactly the same effect; he therefore concluded that the action of strophanthin depended entirely upon the concentration of the drug, and was not influenced by the total quantity of the drug present.

I investigated this question with the apparatus already described, using quantities of fluid varying from $\frac{1}{2}$ c.c. to 100 c.c. With the varying quantities of fluid the minimal concentration of digitoxin was ascertained which, within one hour, would produce a systolic effect from which the heart did not recover (fig. 2). From these results it will be seen that if quantities of fluid varying from 2 c.c. to 100 c.c. are used the minimum lethal concentration of the drug remains constant, but when smaller quantities of fluid are used slightly higher concentrations are required to produce systole. This rise in concentration, although slight, is nevertheless quite definite, and is greater than

can be accounted for by the fact that when small quantities of perfusion fluid are used the volume of the heart muscle may cause some error in calculating the dilution. The weight of the heart of a 25-grm. frog was found to be only 0.06 gr.

A few experiments were performed with strophanthin; the minimal lethal concentration was found to be between 0.0005 and 0.00025 mgrm. per cubic centimetre.

I find the minimal concentrations of digitoxin and strophanthin, which produce systole, to be much lower than the figures obtained by Werschinin with these drugs.

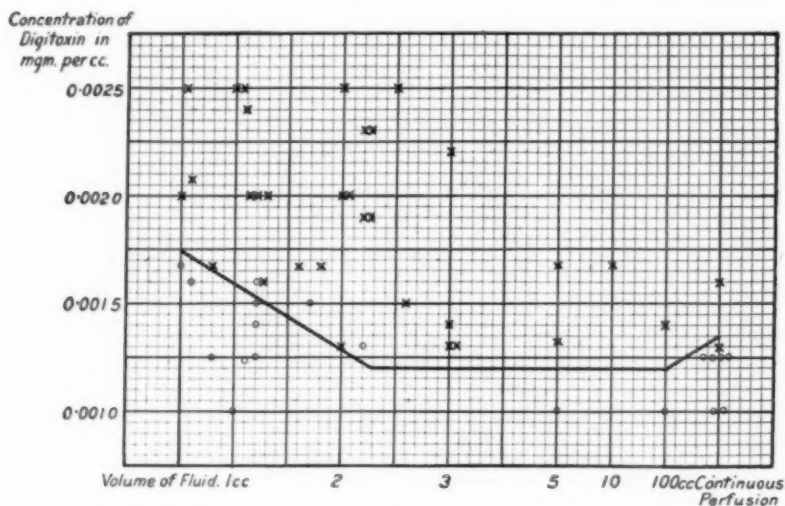


FIG. 2:

This figure shows the minimal concentration of digitoxin which will produce systolic arrest in an isolated frog's heart; it also shows how this minimal concentration varies when the quantity of perfusion fluid is altered. X, systolic effect produced upon frog's heart within sixty minutes, and subsequent death of the heart in systole; O, no systolic effect produced, or slight systolic effect followed by recovery.

(III) DIASTOLIC EFFECT OF DIGITALIS GLUCOSIDES.

Werschinin [10] follows Schmiedeberg in describing a diastolic effect produced by the digitalis glucosides in low concentrations, and in some of his work he takes considerable pains to ascertain the minimal concentration of strophanthin that will produce a systolic, as opposed

to a diastolic arrest. Straub [7] denies that the digitalis glucosides have any diastolic action, and ascribes the diastolic effects observed by Werschinin to instrumental error, for he points out that Williams's apparatus, which was used by Werschinin, produces an excessive diastolic pressure. I agree with Straub's conclusion; the lowest concentrations of digitoxin and strophanthin that have any action produce at first a systolic effect, but the heart may partially recover from systole and continue beating slowly and regularly for some hours, finally dying in semi-systole: this occurs most frequently when large quantities of fluid are passed through the heart (fig. 3). If such a heart were

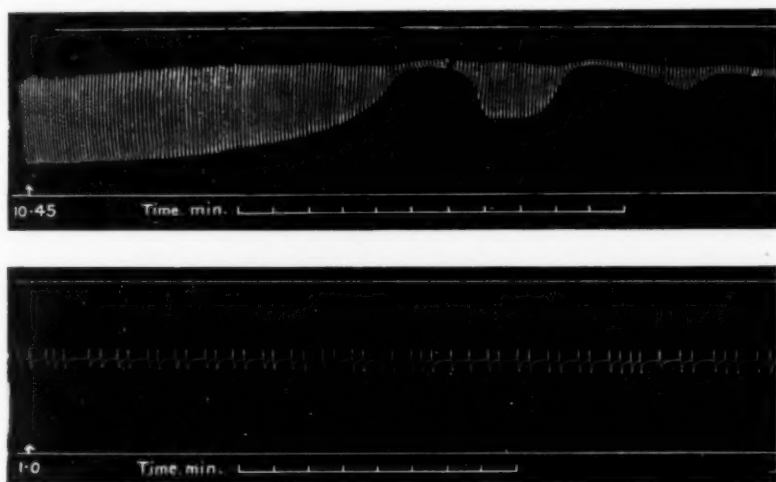


FIG. 3.

Isolated frog's heart perfused with 150 c.c. Ringer's fluid, containing 0.00125 per mille digitoxin; an initial systolic effect is produced, followed by partial recovery. There is an interval of two hours between the two tracings. (Tracing reads from left to right.)

subjected to an excessive diastolic pressure it would probably die in complete diastole. In some instances where very minute quantities of drug were used the heart, after showing an initial systolic effect, recovered completely and maintained a strong regular beat for many hours (fig. 4). Hearts which, before any drug was added, were beating feebly or irregularly, often were rapidly arrested in diastole after the addition of digitoxin, but this never occurred with healthy hearts.

I consider, therefore, that the diastolic effect, described by Werschlin, is due to instrumental error, and that the distinction he draws between the systolic and diastolic effect of strophanthin is not of any importance.

(IV) THE ABSORPTION OF DIGITALIS GLUCOSIDES BY THE
FROG'S HEART.

Straub [7] investigated this question by transferring 1 c.c. of fluid containing 0.0025 mgrm. of strophanthin through a series of hearts. After passing the fluid through six hearts a marked diminution in its

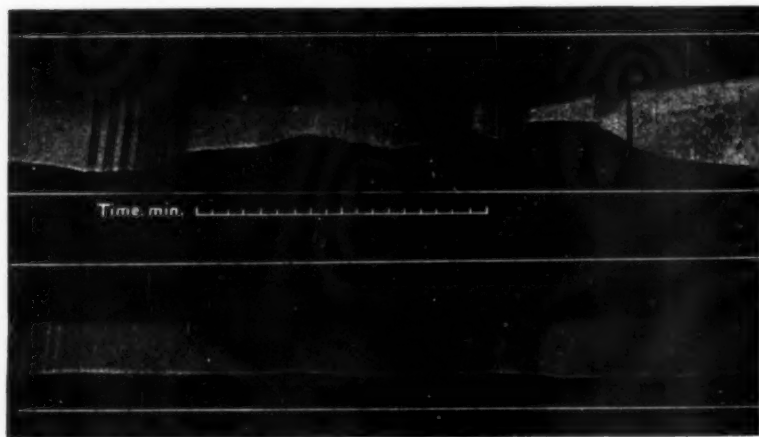


FIG. 4.

Isolated frog's heart perfused with 0.5 c.c. of Ringer's fluid containing 0.00083 mgrm. digitoxin; initial systolic effect produced, which is followed by a complete recovery. (Tracing reads from right to left.)

action was observed, and Straub calculated that each heart absorbed 0.0002 mgrm. of the drug. Using digitoxin I obtained the following results: 2 c.c. of Ringer's fluid, containing 0.005 mgrm. digitoxin, were passed successively through three frog's hearts perfused by Straub's method. The first heart died in systole in thirty-seven minutes; the second heart died in systole in thirty-six minutes, but no systolic effect was produced upon the third heart.

Now a concentration of 0.0012 mgrm. per cubic centimetre of digitoxin produces a systolic effect, therefore the fluid at the end of

the experiment must contain less than $2 \times 0.0012 = 0.0024$ digitoxin. Therefore the two hearts must have absorbed 0.0026 mgrm.; therefore each heart must have absorbed 0.0013 mgrm. of digitoxin.

Using strophanthin I obtained the following results: 1 c.c. of Ringer's fluid containing 0.00066 mgrm. strophanthin was passed successively through four frog's hearts which were perfused by Hartung's method. The first heart died in systole in twenty minutes; the second heart died in diastole in ten minutes; the third heart died in systole in sixty minutes, but no systolic effect was produced upon the fourth heart.

Only 0.7 c.c. was recovered at the end of the experiment, some fluid being lost between Nos. 2 and 3.

Now strophanthin in a concentration of 0.0002 mgrm. per cubic centimetre just fails to produce a systolic effect, therefore not more than 0.0002 mgrm. was present at the end of the experiment; 0.3 c.c. fluid was lost, which corresponds to 0.00020 mgrm.; therefore three hearts absorbed $0.00066 - 0.0004 = 0.00026$ mgrm., and therefore each heart absorbed about 0.00008 mgrm. of strophanthin. Since the strophanthin I used was about four times as toxic as the gratus strophanthin used by Straub, this figure agrees with his result.

Using digitoxin, a much higher absorption figure was obtained, but the experiment took four hours to carry out, and it was found that dilute solutions of digitoxin in Ringer's solution suffered a very marked loss of strength on standing many hours; therefore the absorption figure for digitoxin is very possibly inaccurate.

(V) OTHER FACTORS INFLUENCING THE ACTION OF DIGITALIS GLUCOSIDES.

Trendelenburg [8] investigated the length of time taken by strophanthin to kill the isolated frog's heart; he found that all concentrations between 0.25 and 0.005 mgrm. per cubic centimetre took the same time to kill the heart—namely, ten minutes, but weaker dilutions took a steadily increasing time. Schmiedeberg [6] found with gratus strophanthin that 0.003 mgrm. per cubic centimetre took thirteen minutes, 0.002 mgrm. per cubic centimetre took twenty-five minutes, and that 0.001 mgrm. per cubic centimetre took thirty-two minutes to kill a frog's heart, using Williams's apparatus. I found that the time at which a heart died—that is to say, the time at which the last spontaneous beat occurred—varied very greatly, but that the time taken to

produce a maximal systolic effect was roughly proportional to the degree of dilution (fig. 5).

The effect of concentrations above 0.004 mgrm. per cubic centimetre was not investigated.

The effect on the heart of digitalis glucosides in high concentrations is a permanent one, and the heart cannot be restored to activity by washing out, but Straub showed that with weak concentrations the heart after it had been arrested in systole could be restored to activity by washing out with Ringer's fluid. I tried the effect of washing out the heart with Ringer's fluid at various stages of digitoxin poisoning. If 0.003 mgrm. per cubic centimetre of digitoxin is allowed to act on

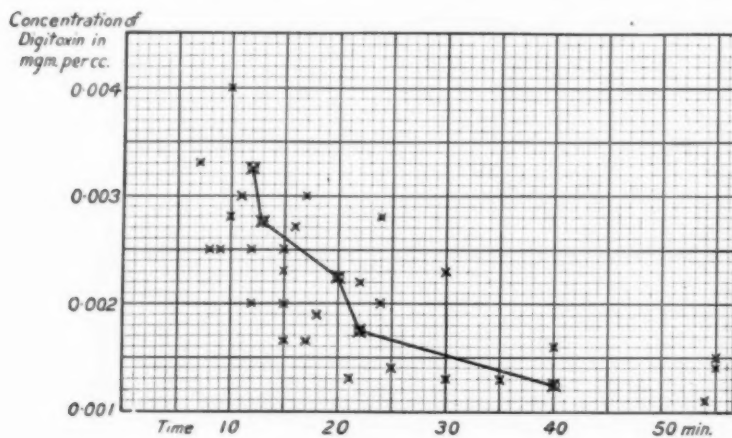


FIG. 5.

Curve showing the times at which different concentrations of digitoxin produce their maximal systolic effects upon isolated frogs' hearts.

X = single observation, **X̄** = average of a group of observations.

the heart for less than five minutes, and then the heart is washed out, no systolic effect follows; but if the digitoxin is allowed to act for eight minutes, and is then washed out, a systolic effect occurs (fig. 6). This systolic effect occurring after the digitoxin has been removed suggests that either digitoxin enters into some form of combination with the muscle from which it can only be slowly removed by washing out the heart, or else that the digitoxin initiates some slowly developing change in the heart muscle, which change can be continued in the absence of the drug. In fig. 4 it will be seen that when a very small amount

of digitoxin is used the heart may develop a partial systole, and then recover without any of the drug being removed; this can only be explained by supposing that the heart either acquires a tolerance for, or else destroys, the drug.

(VI) THE MODE OF ACTION OF DIGITALIS GLUCOSIDES.

Straub found that only minute traces of strophanthin were absorbed by hearts upon which it acted, and that the action depended entirely

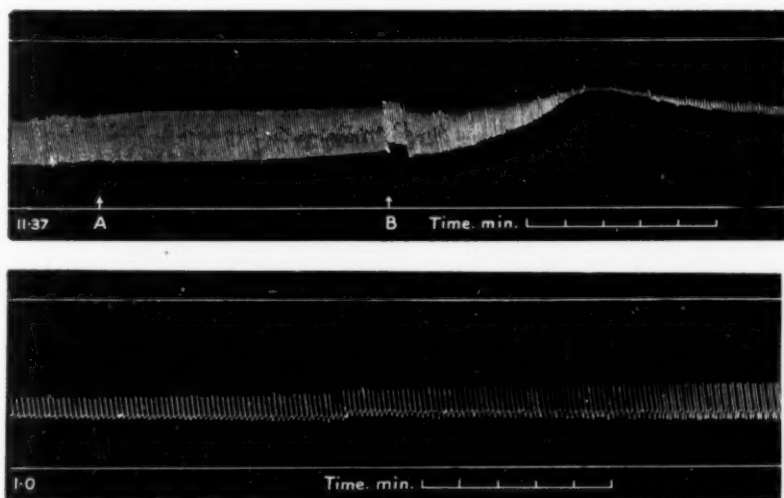


FIG. 6.

Isolated frog's heart perfused with 3 c.c. Ringer's fluid. **A**, 0.01 mgrm. digitoxin introduced; **B**, heart washed out with Ringer's fluid. Interval of one hour between the two tracings. (Tracing reads from left to right.)

upon the concentration of the drug; from these facts he concluded that strophanthin could not act by entering into combination with the heart muscle, and he suggested that its action was of a physical nature, possibly connected with an alteration of the surface tension. I agree with Straub's facts, except that I find that with minute quantities of fluid the action is slightly modified by the total quantity of drug present. I do not consider that these facts exclude the possibility of a chemical action. The amount of the drug taken up by the heart was very small,

but in the case of strophanthin I found it was at least one-quarter of the amount which would kill a heart if introduced in 1 c.c. of fluid. Straub also found that 0.001 mgrm. of strophanthin in $\frac{1}{2}$ c.c. of fluid killed a heart in systole, and that 0.0002 mgrm. was taken up by each heart. On the other hand, a chemical union between the heart muscle and the drug is certainly suggested by the fact that systolic effects, due to the action of digitoxin, may first appear when the digitoxin is no longer in contact with the heart, as is shown in fig 6.

(VII) THE EFFECT OF ALTERATIONS IN THE COMPOSITION OF THE PERFUSION FLUID.

(A) The effect of reducing the osmotic pressure of the perfusion fluid was first investigated.

(a) Ringer's fluid diluted with an equal volume of water. The minimal lethal concentration of digitoxin was raised slightly.

(b) Ringer's fluid (NaCl half normal concentration, other constituents of Ringer natural). The minimal lethal concentration of digitoxin was raised slightly.

TABLE II.—ACTION OF DIGITOXIN WHEN THE RINGER'S FLUID IS DILUTED.

Number of experiment	Fluid used	Volume of cannula	Concentration of digitoxin	Effect
2.xv.8	Ringer diluted one-half	c.c. 0.75	0.004	Systolic effect in seven minutes; partial recovery; death in semi-systole in four hours
2.xv.9	Ditto	0.65	0.003	Systolic effect in fifteen minutes; partial recovery; death in semi-systole in three hours
2.xiv.3	Ditto	0.9	0.002	Slight systolic effect in twenty minutes; complete recovery
2.xv.7	Ditto	0.5	0.0016	No effect
2.xxi.1	Ringer, NaCl 0.3 per cent.	1.0	0.0025	Systolic effect in thirty minutes; recovery

(B) Effect of altering the concentrations of ions, the osmotic pressure being kept constant.

(a) Diminution in the concentration of NaCl. The osmotic pressure was kept equal to that of normal Ringer by the addition of cane-sugar; 6 per cent. of cane-sugar exercises an osmotic pressure equal to 0.65 per cent. of sodium chloride. In all these experiments large quantities of fluid were perfused through the heart.

TABLE III.—ACTION OF DIGITOXIN IN RINGER'S FLUID, NaCl DIMINISHED, CANE-SUGAR ADDED IN SUFFICIENT QUANTITY TO MAINTAIN NORMAL OSMOTIC PRESSURE.

Number of experiment	Composition of fluid	Concentration of digitoxin in milligrammes per cubic centimetre	Effect
2.XXV.7	Ringer, NaCl 0.26 per cent.	0.001	Systolic effect in ten minutes; complete recovery
2.XXV.3	Ditto	0.00125	Systolic effect in twenty minutes; complete recovery
2.XXVI.2	Ditto	0.00125	Systolic effect in forty minutes; death in semi-systole in a hundred and thirty minutes
2.XXV.1	Ringer, NaCl 0.13 per cent.	0.001	No systolic effect
3.XXVI.4	Ringer, NaCl 0.1 per cent.	0.0016	Ditto
4.0.1	Ditto	0.002	Systolic arrest in sixty minutes

If the NaCl was reduced below 0.1 per cent. the heart no longer maintained a steady beat. From the above table it will be seen that reduction of the NaCl content to 0.1 per cent. has no marked effect upon the action of digitoxin; the diminution in the toxicity of the digitoxin observed when the Ringer was diluted and no cane-sugar added must have been due to alteration of the osmotic pressure, and not to diminution in the concentration of the sodium ions.

(b) *Diminution of the Concentration of the Calcium Ions.*—If calcium-free Ringer is perfused through the heart the beat becomes steadily feebler and finally the heart is arrested in diastole; but if calcium-free Ringer is perfused through the heart until the beat is very feeble, and then circulation, with a small quantity of fluid, is established, the heart

TABLE IV.—ACTION OF DIGITOXIN IN CALCIUM-FREE RINGER.

Number of experiment	Concentration of digitoxin in milligrammes per cubic centimetre	Effect
2.XXII.4.	0.004	Systolic arrest in twenty minutes
2.XXVIII.3.	0.004	No systolic effect in thirty minutes
3.GG.1.	0.003	No systolic effect in sixty minutes
2.XXIII.3.	0.003	No systolic effect in one hundred and eighty minutes
2.XXII.2.	0.0023	No systolic effect in two hundred and forty minutes
2.XXII.2.	0.0023	No systolic effect in sixty minutes

will maintain this feeble beat for many hours; if digitoxin is now added it causes a stronger beat but no systolic effect is produced unless the concentration is more than twice the concentration that is sufficient to kill a heart in ordinary Ringer's fluid.

But if a little calcium is added to one of these hearts upon which the digitoxin has acted for some time, immediate systolic arrest occurs. Moreover, if the digitoxin is allowed to act upon the heart for some time and then the heart is washed out for ten minutes with calcium-free Ringer containing no digitoxin and then a little calcium is added,

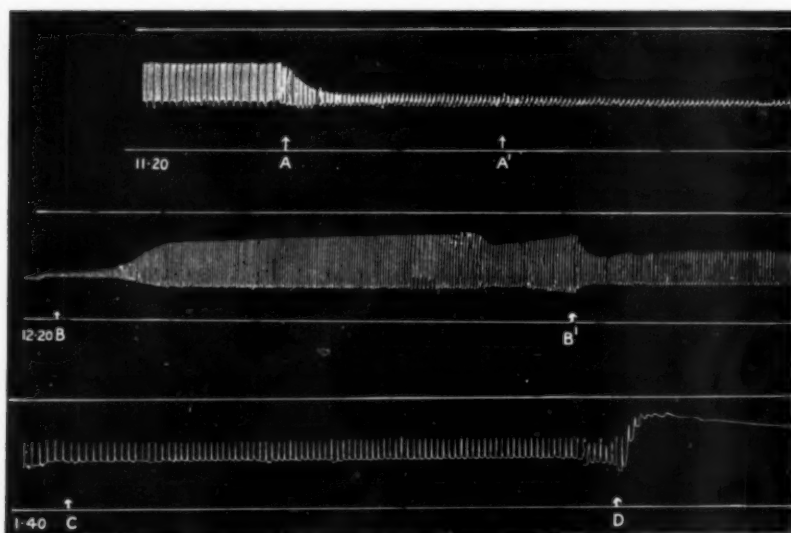


FIG. 7.

Tracing of isolated frog's heart. At **A**, perfused with Ringer's fluid containing no calcium; at **A'**, perfusion stopped and circulation of 3 c.c. of fluid established; at **B**, a trace of calcium chloride added; at **B'**, 0.01 mgrm. digitoxin added; at **C**, washed out with Ringer containing no calcium; at **D**, calcium chloride added to make 0.02 per cent. (Tracing reads from left to right.)

immediate systolic arrest occurs (fig. 7). From the figure it will be seen that the systolic arrest is not in the least like the systolic arrest produced by digitalis, but closely resembles the systolic arrest produced by barium chloride. A similar systolic effect is produced by adding calcium to a heart beating in 0.65 per cent. NaCl., but no similar effect can be produced by adding calcium even in excess to a heart beating in

calcium-free Ringer unless the heart has been acted upon by one of the digitalis glucosides. It is, of course, impossible to free the heart entirely of calcium, but it would appear that digitalis acts upon the heart in such a way that when calcium is present the muscle contracts into systole, but that when calcium is absent systolic contraction cannot occur.

(c) *Calcium in Excess.*—Werschinin found that excess of calcium increased the systolic action of strophanthin, with normal Ringer 0.01 mgrm. per cubic centimetre of strophanthin was required to produce systolic arrest, but if the calcium content were increased to 0.09 per cent. then 0.002 mgrm. per cubic centimetre of strophanthin would produce systolic arrest. I found that increasing the calcium content above normal did not greatly affect the toxic action of digitoxin.

TABLE V.—ACTION OF DIGITOXIN IN PRESENCE OF EXCESS OF CALCIUM.

Number of experiment	Volume of cannula	Concentration of calcium	Concentration of digitoxin in milligrammes per cubic centimetre	Effect
3.M.3.	2.0	0.1 per cent.	0.002	Death in systole in twenty minutes
2.xxxvii.2.	3.2	0.1 „	0.0013	No systolic effect
3.J.1.	2.5	0.12 „	0.0008	Death in semi-systole in one hundred and twenty minutes

Excess of calcium does not increase the toxic action of digitoxin. The percentage of calcium in Ringer's solution is about the optimum for an effective digitalis action.

(d) *Effect of diminishing the Concentration of the Potassium Ions.*—The heart usually would not maintain a regular beat in Ringer's solution without potassium, even when only a small volume of fluid was used, but when a regular beat did occur the action of digitoxin was slightly increased by the absence of potassium.

(e) *Effect of increasing the Concentration of the Potassium Ions.*—Increase in the amount of potassium present slightly diminished the action of digitoxin.

Alterations in the concentration of potassium do not appear markedly to influence the action of digitoxin.

(f) *Effect of altering the Alkalinity of Ringer's Fluid.*—Excess of alkali slightly increased the activity of digitoxin. If no alkali was present and the fluid was made faintly acid with lactic acid there was

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TABLE VI.—SHOWING EFFECT OF VARYING THE CONCENTRATION OF POTASSIUM.

Number of experiment	Concentration of potassium chloride	Concentration of digitoxin in milligrammes per cubic centimetre	Effect
2.XXVII.3	<i>Nil</i>	0.002	Death in diastole in twenty-two minutes
2.XXVII.5	„	0.001	Death in systole in twenty minutes
2.XXX.2	„	0.0008	Death in systole in thirty-eight minutes
4.II.2	0.2 per cent.	0.004	Systolic arrest in ten minutes
2.36.1	0.04 „	0.0027	No effect in three hundred minutes
3.M.6	0.2 „	0.0025	Slight systolic effect followed by recovery
3.FF.3	0.2 „	0.0025	Systolic arrest in twenty minutes
4. S. 1	0.2 „	0.002	Systolic arrest in forty minutes
4. S. 2	0.1 „	0.002	Diastolic arrest in forty minutes

immediately a great diminution in the strength of the beat, and the heart often died in diastole, some hearts survived, and to these digitoxin was added. The presence of acid sometimes prevented systole occurring, but did not prevent the digitoxin killing the hearts, which died in diastole.

TABLE VII.—EFFECT OF EXCESS OF ALKALI OR PRESENCE OF LACTIC ACID UPON THE ACTION OF DIGITOXIN.

Number of experiment	Perfusion fluid	Concentration of digitoxin in milligrammes per cubic centimetre	Effect
3.J.1.	Na_2CO_3 0.1 per cent.	0.001	Systolic arrest in thirty minutes
3.O.2.	„ 0.15 „	0.001	Systolic arrest in one hundred and twenty minutes
3.D.1.	Lactic acid 0.09 per cent.	0.0018	Systolic arrest in twenty-five minutes
3.D.5.	„ 0.02 „	0.0016	Diastolic arrest in thirty minutes
3.E.1.	„ 0.045 „	0.0016	Diastolic arrest in sixty-four minutes
3.D.7.	„ 0.045 „	0.001	No effect

The presence of acid does not therefore increase the action of digitoxin, nor does it protect the heart, but it may cause the heart to die in diastole rather than in systole.

(VIII) THE ACTION OF THE DIGITALIS GLUCOSIDES IN THE PRESENCE OF BLOOD SERUM.

Werschinin [9] investigated the action of strophanthin upon the heart, both in the presence of blood serum and also in the presence of certain isolated constituents of the serum. He determined the minimal concentration of the drug which would produce systolic arrest in the various fluids employed. He found that 0.01 to 0.008 mgrm. of strophanthin per cubic centimetre was required to produce systolic arrest in Ringer's solution, but that one-tenth this concentration (0.001 mgrm. per cubic centimetre) would produce systolic arrest if blood serum was added to the Ringer. He also found that the minimal lethal concentration was reduced, in a less marked manner, after the addition of washed rabbits' red blood corpuscles, of lecithin, of alcoholic solution of the lipid substances of the blood serum, or, finally, of excess of calcium. Using the serums of various animals I have obtained the following results:—

TABLE VIII.—ACTION OF DIGITOXIN AND STROPHANTHIN IN PRESENCE OF SERUM.
Hartung's apparatus—cannula 1 to 3 c.c.

Number of experiment	Fluid used	Drug	Concentration of digitoxin in milligrammes per cubic centimetre	Effect
3.8.5	Frog's serum ...	Digitoxin	0.0026	Systolic arrest in one hundred and twenty minutes
4.N.7	Dog's serum, two-thirds; aqua dest., one-third	"	0.001	Slight systolic effect followed by complete recovery
3.L.3	Frog's serum ...	Strophanthin	0.001	Systolic arrest in one hundred minutes
3.P.3	Ditto	"	0.001	Systolic arrest in sixty minutes
3.EE.2	Ditto	"	0.00025	No systolic effect
3.F.2	Rabbit's serum, two-thirds; aqua dest., one-third	"	0.0023	Systolic arrest in ninety minutes
3.F.3	Ditto	"	0.0023	Systolic arrest in one hundred and twenty minutes
3.F.1	Ditto	"	0.0015	Systolic arrest in one hundred and twenty minutes
3.G.3	Ditto	"	0.001	Systolic arrest in one hundred and fifty minutes
4.r.2	Cat's serum, two-thirds; aqua dest., one-third	"	0.00025	No systolic effect

The serum in these experiments was obtained by centrifugalizing fresh defibrinated blood. As will be seen, the action of both digitoxin and strophanthin was almost unaltered by the addition of serum, the minimal concentration of the drug causing systolic arrest was the same when dissolved in serum as when dissolved in Ringer's fluid, the only difference being that the arrest took rather longer to develop.

This result is very different from that obtained by Werschinin, but I believe this writer's results were due to instrumental error caused by the excessive diastolic pressure of the Williams's apparatus, for this tends to force any feebly beating heart into a condition of diastolic standstill; but a frog's heart to which serum has been added is in a much more vigorous condition than one perfused by saline alone, hence in a Williams's apparatus a dose of strophanthin given with serum will cause a heart to contract into systole, whilst the same dose given with saline produces an apparent diastolic arrest. With the apparatus that I used the diastolic pressure was low, and hence there was no difference between the action of strophanthin in serum or in saline.

SUMMARY.

- (1) The action of digitoxin depends entirely upon the concentration of the drug, except when very small quantities of fluid are used.
- (2) Digitoxin and strophanthin have no diastolic action upon a frog's heart perfused in the manner described in this paper.
- (3) When digitoxin and strophanthin act on the frog's heart only minute quantities are absorbed, but the quantity is not so minute as to exclude the possibility of chemical combination between the drug and the heart muscle.
- (4) The systolic action of digitoxin upon the frog's heart is dependent upon the presence of calcium.
- (5) Diminution in the quantity of calcium in the Ringer's fluid diminishes the systolic action of digitoxin.
- (6) The presence of excess of alkali or the absence of potassium slightly increases the systolic action of digitoxin.
- (7) The presence of excess of calcium, or of blood serum, does not influence the systolic action of digitoxin.

Addendum.—Since the above article was written Grünwald [1] has published a paper dealing with the absorption of digitalin pur. (Merck) by the frog's heart perfused in Williams's apparatus. He found that the minimal concentration of digitalin which produced systolic

arrest was 0.026 per mille; Werschinin [9] found the corresponding concentration of digitoxin was 0.01 per mille; digitalin is therefore about one-third as toxic as digitoxin. But Grünwald found that after perfusing 50 c.c. of a solution containing 1.3 mgrm. of digitalin through five hearts in succession a loss of toxicity occurred which corresponded to 0.07 mgrm. of digitalin per heart, and this would correspond to over twenty times the amount of digitoxin that I found was destroyed by a frog's heart. The figure obtained by Grünwald may possibly be due to dilute solutions of digitalin in Ringer losing strength on standing, in the same way that I found to occur with digitoxin. Grünwald also found that if hearts were perfused continuously, systolic arrest was produced by about one-half of the concentration of digitalin that was required to produce arrest when the fluid was circulated. This result appears very extraordinary, for I found that the concentration of digitoxin which was required to produce arrest was slightly higher when large quantities of fluid were perfused than when small quantities (e.g., 3 c.c.) were circulated.

I desire to take this opportunity to express my thanks to Professor Dixon for his valuable help, and advice, given during the course of these experiments.

[The expenses of this research were in part defrayed by a grant from the Royal Society.]

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- [10] *Idem.* *Ibid.*, 1910, lxiii, p. 386.

DISCUSSION.

The PRESIDENT (Professor W. E. Dixon, F.R.S.) said that the contribution contained many points new to him. First, Dr. Clark had thrown light on the question of how digitalis produced its effect. Straub contended that it was a matter of concentration, that digitalis, in other words, produced its action by some physical action, and that this action was directly proportional to the degree of concentration of the digitalis. But according to Dr. Clark this was not strictly true, so that the law previously enunciated held good only to a limited extent. It was clear that the total quantity of digitalis in the fluid was also an important factor to remember. The other point which he regarded with considerable interest was that if the frog's heart was perfused with digitalis or strophanthus until it was killed in systole, that heart had not taken up enough digitalis or strophanthus from the perfusing fluid to produce any decided action on another heart. It did not look to him, in view of this fact, as if the systolic standstill could be entirely a chemical phenomenon. If it were, one would surely expect the heart to take up enough digitalis from the solution to produce a decided physiological effect on another heart. As a matter of fact, the frog's heart specifically absorbed such a small quantity of digitoxin that it was within the range of experimental error. The last point he desired to refer to was that concerning calcium. Dr. Clark's experimental results in regard to that were most important, namely, that digitalis in three or four times a lethal dose produced little or no effect on the heart unless calcium was present, and that if digitalis in a calcium-free saline were perfused through a heart, it would go on beating for hours until a small quantity of calcium was given. Then the moment calcium was added the heart went into tonic contraction. He hoped that Dr. Clark might be able to tell them something as to the significance of this phenomenon.

Dr. H. H. DALE said he was impressed with this departure from Straub's rule as to the independence of the effect on volume, and its dependence solely on the degree of concentration when very small volumes were used. When one put the small volume into the frog's heart that organ was wet, it had not been dried, and so the interstices were filled with blood and serum. And if it were washed out with small quantities of Ringer's solution there must be an effect of dilution. That might be inappreciable when employing a considerable volume, but when using a small quantity it would be appreciable, and the smaller the quantity the greater would be the effect of that dilution. He wondered whether this was a valid criticism of Dr. Clark's contention that, with a very small volume one found a departure from Straub's rule.

Professor CUSHNY, F.R.S., said that he believed there was a curious diastolic effect in digitalis which Dr. Clark had not observed. If one gave a frog a minimal dose of any one of the digitalis series and opened the chest

afterwards, when the circulation had ceased one would often find the heart in diastole, and it was constant if the dose was the smallest quantity which would stop the heart. But if one touched the heart, with the scissors or with a pin, one caused it to go into systole; not the whole heart, but if one drew a line with the pin along the diastole one would find a white line following upon the pin. There was a diastolic effect apart from the systolic, which was not an inhibitory phenomenon, because it occurred under atropine. Of course Straub did not get this, and he supposed that Dr. Clark did not get it either, because they had employed the perfused heart, and the cannula had the same effect as the pin. If one had an intact frog it would be found that the heart stopped in diastole. This was an old observation, which was not seen nowadays, because everyone used the heart attached to something which irritated it. But the early observers all saw this diastole effect. It was described forty years ago by Boehm. And Straub's idea that digitalis did not enter into combination with the heart was robbed of much of its significance, because digitalis or strophanthus acted in such inordinately small quantities—the amount which acted on the human heart was extremely small; $\frac{1}{4}$ mgrm. was distributed through the human body and yet it was sufficient to change the heart in an extraordinary way. The quantity was so minute that it could not be detected chemically.

DR. CLARK, in reply, said he had not known about the heart dying in diastole as mentioned by Professor Cushny. With regard to the question of absorption of strophanthin, this was rather one of figures. The amount of strophanthin absorbed was considerably smaller than the amount of the drug required to kill a heart, even if only $\frac{1}{2}$ c.c. or $\frac{1}{4}$ c.c. of fluid was used. This was the line Straub took up, that if one used such a small amount of fluid one could just kill the heart with a certain dose of strophanthin, but the amount which the heart took up was smaller than this dose of strophanthin. With regard to the question of the volume of the heart, the way in which he estimated the quantity of fluid was at the end of the experiment to weigh the heart and cannulae with their contained fluid, then to empty and dry the heart and cannulae, and weigh again, thus obtaining the weight of the fluid; in this way he was able to ascertain exactly the amount of fluid. The weight of the moist frog's heart was 60 mgrm., but the smallest quantity of fluid he used was 500 mgrm., so that the volume of heart was only 12 per cent. of the volume of the fluid. The minimal concentration of digitoxin which would kill a heart with only $\frac{1}{2}$ c.c. of fluid was 0.0018 per cent., whereas with 3 c.c. the minimal concentration was 0.0012 per cent., so there was a difference of 33 per cent. between the lethal doses. These doses were so very small that one did not like to be too sure; it was so easy to have a slight error in that way. He was convinced that there was a definite increase in the concentration of digitoxin required to kill the heart when quantities of fluid below 1 c.c. were used.

The Action of the Digitalis Series in Heart Disease.

By A. R. CUSHNY, M.D., F.R.S.

WHEN Dr. Mackenzie and his pupils and myself began working on the action of digitalis and its allies at Mount Vernon, the first point was to find out whether the substitutes for digitalis were equally valuable; whether there were special indications for digitalis as opposed to those for squill and strophanthus. And in a former communication to the Section¹ I pointed out that there was very little evidence that strophanthus or squills were preferable in any case to digitalis, which is much more certain in its action; but that, on the other hand, strophanthus might be substituted for digitalis in any special case. There is no essential difference in the action of any of the three on patients. The second point which we took up was to develop the statement made by Mackenzie some seven years ago that digitalis acted specially on the cases which we know as auricular fibrillation. That has been fully confirmed in a paper recently published by Mackenzie in *Heart*.² The third point that we took up was, how did digitalis act, how far was the action due to its direct action on the heart, and how far was it due to an inhibitory effect, that is, to action upon the inhibitory centre? That point has been specially worked upon by Silberberg and Marris and myself. Silberberg has already read a preliminary note on this subject before this Society,³ and a full paper will soon appear in *Heart*.

The first thing to do in any investigation of this kind is to determine what is the nature of the heart lesion. We have divided the heart diseases which we have treated into two classes. I shall call those, first, cases of normal rhythm, in which, although there may be some irregularity, the impulses start from the ordinary pacemaker, the auricle beats after the impulse reaches it, and the ventricle beats after the auricle. The other class is that which is known as auricular fibrillation, in which the impulses arise from a very disordered action of the auricle, and the ventricle follows these as well as it may. The reaction to digitalis of these two classes is extraordinarily different. As Mackenzie has pointed

¹ *Proceedings*, 1911, iv, pp. 7-11.

² *Heart*, 1910-11, ii, pp. 273-386.

³ *Proceedings*, 1911, iv, pp. 192-210.

out, in the normal rhythm heart digitalis occasionally slows the beat. It is a comparatively low percentage, about 1 in 5, in which the heart is slowed by digitalis. And the heart in those cases shows all the symptoms of inhibitory activity; there are all the symptoms which one knows accompany stimulation of the vagus centre. The particular forms one sees are, block between auricle and ventricle, and sinus slowing, that is to say, fewer impulses are sent out from the pacemaker in one set, and in the other set fewer impulses pass from auricle to ventricle. In the vast majority of those cases this is a true vagus stimulation, because one can get rid of this irregularity by giving atropine. And in Silberberg's paper you may remember that in all his cases in which the atropine was given and the heart was of normal rhythm, the slowing due to digitalis disappeared, that is to say, slowing was inhibitory in character. Very soon after Silberberg's paper was read we came across two cases in which this did not hold true, as you may see from the lantern slides. Here in normal rhythm hearts slowing and irregularity of the pulse occurred, which did not disappear under atropine, and therefore were not of inhibitory character. Silberberg showed in this paper that in auricular fibrillation the slowing induced by digitalis was not inhibitory, for it did not disappear under atropine. We have continued the work by observations in which strophanthin was injected intravenously and the slowing was noted from hour to hour. Other observations were made on the same patients, but in these, while strophanthin was given intravenously the inhibitory mechanism was put out of action by atropine. In the two sets of observations the heart was slowed in the same way, that is, strophanthin slowed the heart in auricular fibrillation even when the inhibitory mechanism could no longer act. Some of the charts obtained in this way you may see on the screen, and you will observe that the slowing is the same in character whether atropine is given or not.

The slowing of the normal rhythm heart under digitalis is therefore generally, but not invariably, inhibitory in origin. The slowing in auricular fibrillation does not arise from stimulation of the inhibitory centre, and in fact the inhibition is less active during the slow pulse than before or after the digitalis action. Having reached the negative point that the slowing in these cases is not due to inhibition, we think it is worth while recording the fact. But we have scarcely approached the question as to what the slowing is due to. We have got rid of one explanation which has been given, and we are now faced with the difficulty of saying what the slowing arises from. One is inclined to say

it may be a direct action on the bundle, such as we met in the two cases, one of which I showed you, of normal rhythm; that there was failure of conduction in the fibrillation cases from a direct vago-mimetic action. But while it occurs in the frog, he is, after all, a distant relative to the human to argue from, and I tried whether one could find a defect in the passage of impulses in the dog, whether the passage through the auriculo-ventricular bundle was rendered more difficult in digitalis; because we found some years ago that there was often developed in the dog's heart under digitalis an independent rhythm in the ventricle, with persistence of the auricular rhythm, which suggested block in the auriculo-ventricular bundle. As a matter of fact, there is no change in the rate of passage through the bundle owing to digitalis in the dog, except through inhibition. If one paralyses inhibition the rate of passage through the bundle is the same before digitalis, or before strophanthin in particular, as after it. So the dog experiments do not encourage us to believe that the slowing of the pulse in this irregularity in man is due to failure in the passage of impulses through the bundle. On the other hand, another explanation might be that whilst the passage through the bundle is unchanged, the impulse having passed the bundle finds a somewhat unsympathetic ventricle, a ventricle with a low rate of excitability, which fails to respond to it. As a matter of fact, one finds a slight diminution in the excitability of the ventricle in the dog; that is to say, the ventricle stimulation by electrical shocks requires a somewhat stronger shock after strophanthin than before it in a heart freed from the inhibition. But I am not sure that the slowing of the heart is not really a tribute to the action of digitalis in improving the contraction of the heart. The heart in these cases is rapid partly, perhaps, because it is irritable; it is half-starved, and the digitalis, by improving the contraction, may do something by way of improving the nutrition, and thus making the ventricle indirectly less excitable and less receptive for auricular impulses. What suggested this idea to me was that in some of these cases there was a considerable and quite definite fall in the rate of the pulse simply on putting the patient to bed. After this degree of slowing had been maintained for a time we gave digitalis, and it slowed still further. One cannot suppose that the rest in bed led to paralysis of the bundle, or lessened the conductivity of the bundle through direct action. Yet one must suppose that the slowing is of the same character. If digitalis slows the heart by merely improving the nutrition, one would suppose rest in bed would have the same effect. That is the reason I suggest that possibly the slowing is

due to the indirect action of digitalis upon contractility. But this is purely hypothetical. We have, however, a definite problem to solve—the cause of the slowing of the heart and pulse in auricular fibrillation under digitalis, for the old explanation has proved to be incorrect.

DISCUSSION.

The PRESIDENT (Professor W. E. Dixon, F.R.S.) said it was not very often that even this Section had an opportunity of listening to an exposition of experimental therapeutics; this branch of investigation was almost conspicuous by its absence in this country. It was thus a great pleasure to listen to the author's contribution that day, especially as it seemed to him that the experiments he now detailed were fundamental. They all had taught and believed up to the present that digitalis slowed the heart entirely by its vagal action, and that if one gave digitalis or its congeners along with atropine there was an action on muscle without any cardiac slowing. Apparently that was wrong, at all events in some cases of auricular fibrillation. But he would make a suggestion. A number of years ago he was doing experiments consisting of perfusing isolated hearts, when he noticed, while observing the percentage of oxygen in the perfusing fluid acting through the heart, that when one diminished the percentage of oxygen in the perfusing fluid the rate of the heart beat was increased. If that observation were correct, was it conceivable that this might throw some light on the action of digitalis—namely, by sending a better blood through the coronary vessels, so improving the nutrition of the heart, and in that way slowing the heart beat?

Dr. CHARLES W. CHAPMAN said he was interested particularly in the latter part of Professor Cushny's paper in which he said that probably the action of digitalis might be in the direction of improving the nutrition of the muscle. This remark brought him back to what Sir Samuel Wilks always used to teach—namely, that digitalis was not a cardiac depressant but a cardiac tonic. Sir Samuel Wilks emphasized this very strongly at a time when it was not at all generally recognized. It seemed that the profession was returning to that view, from what the President had just said.

Dr. BEZLY THORNE considered that the suggestion made by Professor Cushny was of vital importance from the therapeutical point of view. If digitalis improved the contraction of the heart, it improved the driving power of that organ through the coronary vessels; and if the coronary vessels carried more nutritive material to the myocardium, and the myocardium took a longer swing in its systolic movement, it would probably occupy more time in so doing. It was just possible—though as far as he was concerned it was pure speculation—that this was so. It was known that digitalis improved the tone of the auricle, and consecutively that of the ventricle also. It would

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be very interesting if these experiments showed that digitalis acted mainly by improving the nutrition of the myocardium itself.

Dr. H. H. DALE asked how Professor Cushny could be certain that he had excluded all vagus effect. Was it not possible that the stronger stimulation of the vagus centre under digitalis was able to break through a resistance opposed by atropine, even when this was adequate to block the weaker effect of normal vagus tone?

Dr. LANGDON BROWN said that the paper was most interesting, in that it suggested the consideration of digitalis as a possible improver of cardiac nutrition. He took it that Professor Cushny divided the cases into two groups and that he still held that auricular fibrillation was largely benefited by partial blocking of the passages of the impulses down the auriculo-ventricular bundle. Or did Professor Cushny mean that in this matter we should go back to the beginning?

Professor CUSHNY, in reply, said he had always found that $\frac{1}{50}$ gr. of atropine was sufficient to accelerate the heart before digitalis. In cases of doubt he had given $\frac{1}{25}$ gr. He believed he was right in assuring the Section that he excluded vagus action; at any rate, in some cases pressure on the vagus after atropine had no effect on the pulse-rate. One might suppose, theoretically, that strong stimulation of the vagus might send an impulse through, but that a weak stimulation would not do so. He was not sure whether that was a practicable point. [Dr. DALE asked whether a minute dose of atropine would not block the effect of a very weak electrical stimulation of the vagus, while the effect of a strong electrical vagus stimulation would still pass. If one could assume that any dose of atropine which would block any stimulation would block all, his point fell to the ground.] He did not know that anything on this last point mentioned by Dr. Dale had been done experimentally. In reply to Dr. Langdon Brown, he thought one should start with a clean slate: he was not sure that blocking of impulses was what digitalis did; it might be that it rendered a ventricle less excitable. All that he had so far determined was that it was not an inhibitory block. He was interested in the President's remark that the loss of oxygen made the ventricle more irritable, because he was not aware of any work having been done in which the condition known to the clinician as the irritable heart had been shown experimentally as being present in weak nutrition. He did not suppose that digitalis, in some mystic way, improved the nutrition of the heart; he supposed that digitalis strengthened the beat of the heart, as was universally acknowledged, that this strengthened beat improved the flow of blood through the coronary arteries, and that this led to improved nutrition. The improved nutrition, in other words, was an indirect result of the improved strength of the heart beat.

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PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

Discussion on Syphilis

With Special Reference to (a) Its Prevalence and Intensity in the Past and at the Present Day; (b) Its Relation to Public Health, including Congenital Syphilis; (c) The Treatment of the Disease.

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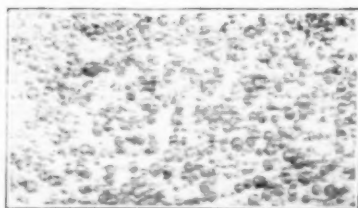
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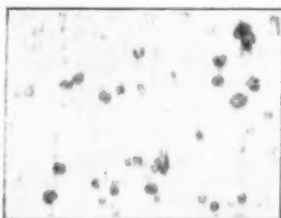
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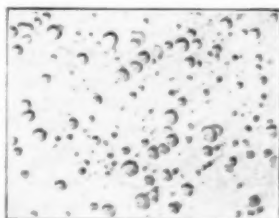
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